

Stig Gårdmark

Studies on Acid-Base Balance,  
Carbohydrate and Lipid Metabolism  
in Human Fetal and Maternal Blood,  
in Clinical and Experimental Conditions  
during Labour

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CARBOHYDRATE AND LIPID METABOLISM  
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- I Gårdmark, S., Jacobson, L. & Rooth, G. A double-blind study of the influence on fetal and maternal biochemistry of paracervical block during labour.
- II Gårdmark, S., Jacobson, L. & Rooth, G. Changes in fetal and maternal acid-base balance and in blood components of the carbohydrate and fat metabolism in 31 cases of fetal bradycardia after paracervical block during labour.
- III Gårdmark, S. & Jacobson, L. The lidocaine concentration in fetal and maternal blood after obstetrical paracervical and pudendal block anaesthesia, respectively, with special regard to its significance in paracervical block fetal bradycardia.
- IV Gårdmark, S., Gennser, G., Jacobson, L., Rooth, G. & Thorell, J. Influence on fetal carbohydrate and fat metabolism and on acid-base balance by glucose administration to the mother during labour.
- V Gårdmark, S., Jacobson, L. & Rooth, G. Fetal and maternal acid-base balance and glucose metabolism during labour in breech presentation.
- VI Gårdmark, S., Jacobson, L. & Rooth, G. Fetal and maternal acid-base balance, carbohydrate and lipid metabolism in relation to different signs of fetal distress during labour.
- VII Jacobson, L., Gårdmark, S. & Rooth, G. Theoretical aspects on the maternal-fetal pH-difference ( $\Delta\text{pH}$ ), determined during labour.



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## GENERAL INTRODUCTION

The introduction of the scalp blood sampling technique (Saling 1962) should be considered an important event in obstetrics, providing new possibilities for biochemical studies of the human fetus during the main course of labour. Numerous reports on the application of this method have appeared. The technique is mainly applied in the diagnosis of fetal distress during labour, focusing the interest on the levels and changes in fetal pH and acid-base balance but, naturally, any blood component for which micro-methods are available could be determined. Studies have thus been reported on, for instance, fetal electrolytes, carbohydrate metabolites, proteins, etc.

The risk for the fetus of this method is practically nil, and only few cases of complications are reported in the literature. The current experience at this Department (Gårdmark and Jacobson) covers approximately 1,500 consecutive fetal scalp blood samplings without any complication.

Despite the great number of publications on fetal scalp blood acid-base balance as an indicator of the oxygenation state of the fetus there are fewer basic investigations of the fetal metabolism in physiological and defined pathological conditions. Still, there are different opinions about, for instance, the clinical significance of various fetal biochemical changes and about compositional standards valid for the fetal scalp blood. The importance of correlating fetal scalp blood determinations with simultaneous maternal blood measurements, stressed by i. a. Jacobson 1970, has often been neglected.

Although many factors, often difficult to ascertain, may influence single determinations in fetal scalp blood, it was clearly shown by Jacobson (1970) that such determinations, carried out in well-defined groups of cases and according to a homogeneous investigative design, might yield reliable physiological and clinical information on specific topics. The present investigation was initiated as a natural continuation and extension of his study, by applying the same methodology on certain clinical and physiological problems, concerned with feto-maternal metabolism during labour, still subjected to divergent opinions or given less attention.

The aim of the present investigation was:

1. To study on a broad biochemical basis and under well-defined conditions the influence of paracervical block on the fetal and maternal metabolism.
2. To study the correlation between fetal bradycardia of different degree after paracervical block and fetal metabolic changes.
3. To measure the blood concentration of a local anaesthetic after paracervical block in mother and fetus and to evaluate the significance of that concentration in the aetiology of fetal bradycardia.
4. To evaluate the representativity and the clinical applicability of fetal blood sampling in breech and foot-breech presentations.
5. To analyse the influence of glucose load to the mother on the fetal acid-base balance and carbohydrate and lipid metabolism, and to elucidate the maternal-fetal interrelationship of the metabolic response.
6. To analyse the metabolic significance of various clinical signs of fetal distress in well-defined series.
7. To compare different biochemical variable(s) in different groups with clinical signs of fetal distress in an attempt to find the variable(s) most informative and feasible for routine clinical practice.

## PARACERVICAL BLOCK DURING LABOUR (I, II, III)

### Background

Paracervical block during labour (blocking the pelvic hypogastric plexus in the paracervical space) has been known since 1926 (Gellert). Because of less effective, short acting, and toxic local anaesthetics, it was a long time before the method was adopted in obstetric practice (Rosenfeld 1945 and Freeman 1950); in fact, it was not until the beginning of the last decade that paracervical block was more generally used during labour.

The enthusiasm and great interest in using the paracervical block as obstetrical analgesia is due to the simplicity in management of the method; it can easily be administered by the obstetrician himself and is effective

and safe for the parturient. However, the rather short duration of the pain relief at single injections limits its value.

Transient fetal bradycardia after paracervical block is from the beginning known to be the main side effect. The significance of this has not been satisfactorily investigated. Single cases of intrauterine fetal death in connexion with paracervical block (see Teramo 1971, Thiery and Vroman 1972) have made many obstetricians hesitate to use it. However, transient fetal bradycardia after the paracervical block was presumed to be rather innocuous until Teramo and Widholm (1967) reported fetal acidosis in connexion with its influence on fetal heart rate. After this first report, further investigations followed which suggested such a relation, (Hickl and Kirchner 1968, Jung et al. 1969, Teramo 1969 a + b, Obelensky et al. 1969, Asling et al. 1970 and Freeman et al. 1972). However, these investigations referred to only a few cases and were based on pH measurements of the fetus only.

The frequency of fetal bradycardia reported after paracervical block was 1-9 per cent up to the end of last decade, but in recent years, figures over 50 per cent have been published (Busch and Lübbert 1970, Teramo 1971, Gårdmark et al. 1972).

The aetiology behind fetal bradycardia is still a matter of dispute. However, the most commonly accepted theory suggests a direct action of the local anaesthetics on fetal heart (Gordon 1968, Hickl and Kirchner 1968, Rosefsky and Petersiel 1968, Teramo and Rajamäki 1971). As a high dose of drug applied as a single injection is reported to give a higher frequency of fetal bradycardia than a lower dose (Teramo and Rajamäki 1971) and higher fetal concentrations of local anaesthetics are found in cases of fetal bradycardia than in cases of uninfluenced fetal heart rate (Gordon 1968, Shnider et al. 1968, Shnider and Way 1968 and Asling et al. 1970), the absolute fetal level of local anaesthetic was considered of great importance. However, as few investigations measure the level of local anaesthetics by specific methods (Holmén et al. 1969, Shnider and Way 1968, Shnider et al. 1968 and Asling et al. 1970) this supposition has not definitely been proved. Other factors, such as constriction of the placental vessels, mechanical compression of the uterine vessels, changes in myometrial activity, and increased pressure on the fetal skull (see Thiery and Vroman 1972), have been suggested as possible causes of fetal bradycardia after paracervical block.

The divergent opinions concerning aetiology and clinical significance of the transient fetal bradycardia after paracervical block initiated the following biochemical studies which started in 1971. At this time, an intensive discussion was going on in Sweden concerning the possibilities



for the parturients to obtain pain relief during labour, and in 1972 the Parliament proclaimed the general right for every woman to receive such pain relief in this country. There was also a great demand from the public for a more general usage of paracervical block during labour, despite many obstetricians being uncertain about the possible negative influence on the fetus.

Against this background and in view of the important relation between maternal and fetal biochemistry, the present investigations are made of different maternal and fetal components of the acid-base balance and of carbohydrate and lipid metabolism under well-defined experimental conditions.

#### A. A double-blind study of the influence on fetal and maternal biochemistry of paracervical block during labour (I)

60 primiparae, all having a normal but painful labour before the block was applied, were investigated by double-blind technique. The aim of this investigations was to study, under well-defined experimental conditions, the following parameters: anaesthetic effect, influence on labour, frequency of fetal bradycardia, conditions of the newborn at birth (Apgar score), and first and foremost, changes in maternal and fetal components of acid-base balance, and of carbohydrate and lipid metabolism.

The 60 women were divided into four groups of 15, receiving: 20 ml 0.5% (100 mg) lidocaine (Xylocain<sup>®</sup>), 20 ml 0.5% lidocaine + epinephrine 1:400,000, 20 ml saline, and 20 ml saline + epinephrine 1:400,000, respectively. Ten ml of these solutions was injected into each lateral fornix at 4 and 8 o'clock with a very short Kobac needle giving an injection depth of 2-3 mm.

Fetal scalp blood and maternal capillary blood were taken before, 20, and 60 min after the paracervical block for simultaneous determinations of pH,  $P_{CO_2}$ , base deficit for the entire extra cellular compartment ( $BD_{ECF}$ ), plasma glucose, lactate, pyruvate,  $\beta$ -hydroxybutyrate, and glycerol.

The amount of local anaesthetic given in this series (100 mg lidocaine) was only half the dose generally used in paracervical block during labour by other investigators. Despite of this and the injection being made at a depth of only 2-3 mm under the vaginal mucosae in order not to cause too rapid absorption into the fetal circulation, the frequency of fetal bradycardia found in this series was high (50 % of the cases receiving lidocaine). No significant difference was noted concerning the incidence of fetal brady-



cardia between groups receiving epinephrine and those not receiving epinephrine. Good anaesthetic effect was found in the groups that received local anaesthetics, 22 out of 30 reported total pain relief and 5 more partial pain relief. Also six patients in the placebo groups reported partial pain relief. No more convincing differences in the progress of labour were noted between the groups.

Four infants in the groups having lidocaine had one-min Apgar score  $\leq 7$  at birth compared with one infant in the other groups, but the 5 min Apgar score was 8-10 in all cases.

In the groups receiving local anaesthetics, the most dominant feature was a decrease in mean maternal and fetal pH 20 min after the block, and the decrease of 0.05 pH units was the same in both mother and fetus. This pH-drop in maternal and fetal blood was caused by an increase in maternal and fetal  $P_{CO_2}$ , and no changes were seen in either maternal or fetal  $BD_{ECF}$  (no signs of metabolic acidosis).

The division of the patients receiving lidocaine into two groups, fetal bradycardia and fetal non-bradycardia groups, showed that the changes in maternal and also in fetal acid-base balance were mainly seen in the bradycardia group. Only slight or no changes were found in the non-bradycardia group. After the division of the material, the following pattern was also seen: mean maternal  $P_{CO_2}$  value in the bradycardia group was lower (22.3 mm Hg), and mean pH value (7.51) was higher in this group before the block was applied than the corresponding values in the non-bradycardia group (mean pH 7.47 and  $P_{CO_2}$  27.4 mm Hg). These findings indicate a strengthened hyperventilation by the mothers before the paracervical block in the bradycardia group. Pain relief in this group caused a maternal increase in mean  $P_{CO_2}$  of 7 mm Hg and a decrease in mean pH of 0.08 units. The fetal changes were about the same amounts and were interpreted as secondary to the maternal changes. Thus the fetal pH-fall in connexion with fetal bradycardia after paracervical block is not usually a sign of metabolic acidosis, as there were no metabolic changes in the fetal  $BD_{ECF}$  and carbohydrate metabolism.

The above-described changes in the acid-base balance were seen at the sampling moment 20 min after the paracervical block, but after 60 min, the mean values of the acid-base status almost returned to the initial level.

Only minor changes were seen in the fetal carbohydrate and lipid metabolism after the paracervical block, even in the bradycardia group. A slight but statistical increase in mean fetal lactate in this group was

noted from 4.0 mmol/l before the block to 6.1 mmol/l 20 min after the block. However, this increase could not be taken as proof of anaerobic metabolism, as an increase in fetal pyruvate was seen concomitantly, giving an unchanged lactate/pyruvate ratio. No significant changes were seen in the maternal carbohydrate metabolism. The most prominent changes in maternal lipid metabolism related to paracervical block was a fall in plasma glycerol seen in the groups receiving lidocaine.

## B. Studies on fetal bradycardia after paracervical block (II)

In addition to the 15 cases of fetal bradycardia in the double-blind series presented above, 16 further cases of fetal bradycardia after paracervical block were investigated in a comparable way. Thus this study comprises a total of 31 cases of fetal bradycardia. In the last 16 cases, a further sampling moment after 10 min after the block was made compared with the double-blind study.

The parameters determined were pH,  $P_{CO_2}$ ,  $BD_{ECF}$ ,  $SAO_2$ , plasma lactate, pyruvate, glucose, and glycerol. In samples drawn at 10 min after the block, only pH,  $P_{CO_2}$ , and  $BD_{ECF}$  were determined.

The aim of this investigation was to study whether more pronounced fetal bradycardia was correlated with biochemical signs of fetal distress. The series was therefore divided into two main groups: A/ moderate bradycardia (19 cases) having fetal heart rate  $> 80$  or  $< 120$  bpm over a period of less than 10 min; B/ Severe bradycardia (12 cases) having a fetal heart rate  $\leq 80$  or  $< 120$  bpm over more than 10 min.

In this series, the results of the double-blind study were confirmed concerning the high maternal mean pH (7.52) and low mean  $P_{CO_2}$  (about 20 mm Hg) before the block was administered in cases where fetal bradycardia occurred after the paracervical block. However in the group of moderate bradycardia, the mean maternal pH drop (0.08 pH units) was more pronounced than the mean fetal (0.05) 20 min after the block. In contrast to this, the fetal pH drop (0.17 pH units) was greater than the maternal (0.06 pH units) in the severe bradycardia group at the same sampling moment. A moderate rise in maternal mean  $P_{CO_2}$  was seen in both groups after the block and also in mean fetal  $P_{CO_2}$  in the moderate bradycardia group, but a higher increase was seen in fetal  $P_{CO_2}$  in the severe bradycardia group from the mean value of 33.5 mm Hg before the block to 52.4 mm Hg 20 min after the block.

In the moderate bradycardia group, a decrease in maternal-fetal pH-difference and only slight changes in fetal  $BD_{ECF}$ , plasma lactate,

lactate/pyruvate ratio, and plasma glycerol were found after the block, making it evident that no biochemical signs of diminished oxygen supply were present in the group of moderate bradycardia after paracervical block; this in contrast to the findings in the severe bradycardia group.

In the severe bradycardia group, maternal-fetal pH difference ( $\Delta\text{pH}$ ) increased and was  $\geq 0.20$  pH units at all sampling moments after the block. This biochemical suggestion of fetal metabolic acidosis was further evident from other biochemical findings. Normally, the fetal  $\text{BD}_{\text{ECF}}$  is below the maternal. The fact that, in the group of severe bradycardia, the mean fetal value exceeded corresponding maternal value 20 min after the block, suggests also a fetal acidosis at this sampling moment. These findings were further confirmed by the increase in plasma lactate and lactate/pyruvate ratio after the block. The increase in fetal plasma glycerol concomitant to a decrease in maternal concentration after the block is interesting in view of earlier observations that report a raised fetal glycerol level in umbilical cord blood in infants depressed at birth. However, these biochemical findings 20 min after the paracervical block was applied were almost restored 60 min after the injection, although the  $\Delta\text{pH}$ , fetal plasma lactate, and plasma glycerol were higher than before the paracervical block was administered.

In addition to the biochemical determinations, the status of the newborn infant was also considered. Only 3 out of the 12 infants in this study with the most pronounced fetal bradycardia had, despite this, an Apgar score  $\leq 7$ . All the infants had a 5 min Apgar score of 8-10.

### C. The significance of fetal and maternal concentration of lidocaine after paracervical block (III)

The study was aimed at further investigating the aetiology of fetal bradycardia after paracervical block in the light of the results found in the double-blind study, which showed high frequency of fetal bradycardia despite the use of small amounts of local anaesthetic. The influence on the fetal heart rate was mainly correlated to the mother's hyperventilating at the moment the block was applied.

The material in this series comprises 23 cases of paracervical and 18 cases of pudendal blocks during labour, 20 ml 0.5 % lidocaine (Xylocain®) being administered in all cases, except in three of the paracervical series, where 15-18 ml was injected. The fetal lidocaine concentration was determined in 100  $\mu\text{l}$  scalp blood sampled 10 and 20 min after the block. In order to investigate the relation between mother and fetus, the concentration of lidocaine was also investigated simultaneously in 5-10 ml

maternal venous blood in 7 of the mothers in the paracervical series and in 13 in the pudendal. The determination of lidocaine was made with a gaschromatographic technique, and the accuracy of the method was high ( $\pm 0.1 \mu\text{g/ml}$  for concentrations  $\geq 0.2 \mu\text{g/ml}$ ).

10 cases of fetal bradycardia occurred after the paracervical blocks. In the fetal bradycardia group, the mean value of lidocaine concentration in fetal blood was  $0.5 \mu\text{g/ml}$  10 min and  $0.4 \mu\text{g/ml}$  20 min after the paracervical block and the corresponding mean values in the non-bradycardia group were 0.4 and  $0.3 \mu\text{g/ml}$ . No significant difference was found between these means. Furthermore, several individual cases in the bradycardia group had the same blood concentration of lidocaine as in the non-bradycardia group. The maternal lidocaine concentration ranges from 0.3 to  $0.8 \mu\text{g/ml}$ , and no difference was found between the cases of fetal bradycardia and non-bradycardia. In no single case did the fetal lidocaine concentration exceed the maternal one.

In the pudendal block series, the mean fetal value was  $0.2 \mu\text{g/ml}$  at both sampling periods, and individual values ranged from  $<0.2$  to  $0.8 \mu\text{g/ml}$ . The mean maternal concentration was 0.4 and  $0.6 \mu\text{g/ml}$  10 and 20 min after the block was applied. In several individual cases in the pudendal block series, the lidocaine concentration by the fetus was the same as in the bradycardia group in the paracervical block series.

Comments. Compared with other investigations some findings in the double-blind study should be emphasized. Despite the injection of a low amount of local anaesthetics, the frequency of fetal bradycardia was high even when an injection depth of 2–3 mm was used. Maternal hyperventilation (low  $\text{Pco}_2$  and high pH) before the block and rapid changes in acid-base status after pain relief (rise in  $\text{Pco}_2$  and drop in pH) were correlated to fetal pH decrease of similar degree and to the occurrence of fetal bradycardia in the presence of local anaesthetics. The maternal and fetal acid-base changes seen 20 min after the block was applied were mainly restored 60 min after the paracervical injection.

The study of fetal bradycardia after paracervical block supports the observation concerning the correlation between fetal bradycardia and maternal hyperventilation before applying the block. Biochemical disturbances of the fetus were found in cases of very pronounced fetal bradycardia, suggesting an impairment of the oxygen supply to the fetus, whereas no changes were seen in cases of moderate bradycardia. The immediate biochemical findings, however, must be seen in view of the fact that most of the infants in the group of severe bradycardia were born vigorously.



Our mean values of the lidocaine concentration were low, both in fetus and mother, after paracervical block compared with other investigators. Furthermore, the mean values of lidocaine concentration in fetal blood did not differ between the fetal bradycardia and non-bradycardia groups, nor were there any substantial differences between the paracervical and the pudendal block series in this respect. The result of this study makes it obvious that factors other than the concentration level of local anaesthetics in the fetus must be important in the aetiology of bradycardia after paracervical block, as discussed above.

## GLUCOSE INFUSION TO THE MOTHER (IV)

### Background

It is generally agreed that carbohydrate provides the main supply of chemical energy and building blocks for biochemical synthesis in the fetus. This opinion has been reached by studies on several mammalian species including primates (see review by Shelley 1968 and Dawes 1968). Glucose and ketone bodies are supposed to cover the metabolic needs also in the human fetus (Šabata *et al.* 1968). Fat is thought to have limited importance as an energy source before birth. This is substantiated by a low concentration of free fatty acids (FFA) and glycerol in fetal scalp blood (Tobin *et al.* 1969) and in cord blood, in contrast to an increased lipid mobilization in newborn immediately after birth with a rise of plasma FFA, glycerol, triglycerides, and ketone bodies (see Persson and Thunell 1971). The role of glucose as the predominant source for fetal intermediary metabolism has, however, recently been challenged (Setchell *et al.* 1972, Battaglia and Mescia 1973). Although amino acids are regarded to be to a certain extent catabolized by the fetus, the list of substances serving as metabolic fuel for the fetus is not yet complete.

Since the role of the heart glycogen as an important factor for fetal survival during hypoxia was established (Dawes *et al.* 1959), glucose infusion to the mother during labour has been widely used with the object of filling the glycogen reserves of the distressed fetus. However, a possible adverse effect of such a treatment has been suggested by findings of accentuated acidosis in asphyxiated lambs after glucose load to the mother (Shelley 1973).

During labour, an increase in maternal glucose concentration is seen (Schönfelder 1965) owing to an augmentation of work-induced glycolysis, which also occasions a rise in plasma lactate and pyruvate. However,

part of the maternal lactate may be anaerobically derived from isometric muscular contractions. The maternal and the fetal plasma lactate concentrations seem to be very close to each other during normal labour, with a parallel increase during the course of labour.

A rise in the basal maternal plasma insulin level in the last trimester is earlier known (Spelacy *et al.* 1963, Bleicher *et al.* 1964) as is the more pronounced insulin response in this part of pregnancy than in the post partum period (Bleicher *et al.* 1964, Spellacy *et al.* 1965). However, insulin release during labour seems to have attracted less attention.

An increase in lipid mobilization has been observed in pregnant subjects (Bleicher *et al.* 1964); also during normal labour, an increased concentration of maternal ketone bodies is reported (Paterson *et al.* 1967; Sabata *et al.* 1968; Persson and Thunell 1971). However, a recent suggestion is that with normal diet no signs of increased lipid mobilization appears during late pregnancy (Persson 1974).

The aim of this investigation was to analyse in some detail the influence of glucose load to the mother on the fetal acid-base balance and the carbohydrate and lipid metabolism, and to elucidate the maternal-fetal inter-relationship of the metabolic response.

The study. Thirteen healthy parturients with normal labour received glucose intravenously early in the first stage of labour. After rapid initial infusion, a steady state of plasma glucose concentration of 180-240 mg% was achieved for one hour. Capillary blood from the mother and scalp blood from the fetus were taken simultaneously before, at the end of, and 30 min after the glucose administration. The following parameters were determined: plasma glucose, lactate, pyruvate, lactate/pyruvate ratio,  $\beta$ -hydroxybutyrate, glycerol, sodium, acid-base components, and haemoglobin. In 8 cases, also maternal plasma insulin was measured.

The hypertonic infusion to the mother did not cause any changes in fetal haemoglobin or sodium concentration indicative of fetal dehydration.

Maternal-fetal difference in glucose concentration increased significantly during the glucose infusion and diminished 30 min after the end of the infusion, when the maternal and the fetal glucose concentration had decreased.

An early maternal insulin response occurred at 3 min after the initiation of the glucose load with a rise of plasma insulin to 112  $\mu$ U/ml, and during the continued glucose administration the insulin level remained around 120  $\mu$ U/ml.

A significant increase in maternal and fetal plasma lactate and pyruvate was found during the infusion, but both the maternal and the fetal lactate/pyruvate ratio remained stable during the study.

Minor changes in acid-base balance were seen; thus the maternal-fetal pH-difference increased to 0.17 pH units 30 min after the glucose infusion.

High maternal levels of glycerol and  $\beta$ -hydroxybutyrate were seen before the beginning of the glucose infusion, and a significant drop was noted after the glucose infusion. A decrease in fetal  $\beta$ -hydroxybutyrate occurred during the maternal glucose load, and contrast to the change in the mother, a rise in fetal glycerol was recorded.

### Comments

The increased difference between maternal and fetal plasma glucose concentration during the glucose infusion to the mother might be attributable to many factors, including a saturation of transport mechanism over the placenta. The rapid maternal insulin response, despite the patients being in labour, suggests that the stress in this part of the labour is not sufficient to block the insulin release.

The importance and the clinical validity of the increased maternal-fetal pH difference when glucose was given is uncertain, and the influence on hypoxic fetuses cannot be judged and call for further investigations.

The high maternal value of plasma glycerol and  $\beta$ -hydroxybutyrate before glucose was given and the decrease after glucose infusion might indicate that the parturients were in a caloric imbalance during their labour. The increase in fetal glycerol during the glucose infusion and the concomitant decrease in maternal glycerol suggests no or slow glycerol passage over the placenta and thus a fetal lipid mobilization already antenatally.

## BREECH PRESENTATION (V)

### Background

The adequate management of breech deliveries is still a matter of dispute, as breech presentation is generally considered to impose an increased risk on the fetus, but different opinions prevail in the literature concerning the perinatal mortality and morbidity rate figures (Todd and Steer 1963, Göbel *et al.* 1971). A 100 per cent use of caesarean section has been advised as a drastic way of managing this obstetrical problem, but it is more common to use caesarean section liberally in breech presentation (particularly in primiparae). Reduction of the perinatal mortality, using high frequency of caesarean section, has been reported, but above a section rate of 26 per cent no difference was found in perinatal mortality between full term infants vaginally delivered by the breech and those delivered by caesarean section (see Dördelman *et al.* 1971). Breech deliveries may often be considered as one type of complicated delivery with higher risk to the fetus than with delivery in occiput anterior presentation. However, rather few reports are available concerning FHR-monitoring and biochemical findings during labour in normal breech deliveries. Earlier, Kubli (1966) studied fetal acid-base in single cases. Eliot and Hill (1972) and Hill and Eliot (1973) have presented the only more comprehensive studies, although they used fetal pH as the only biochemical parameter.

The aim of the present study was to investigate whether fetal blood obtained from the breech or foot in cases of breech or breech-foot deliveries is as representative for the blood of the systemic circulation as is the fetal scalp blood, and to study the fetal biochemistry in normal breech deliveries compared with a control group of normal deliveries in the vertex presentation.

### The present study

Fifteen obstetrically normal breech delivery cases were studied. The infants were all born in a vigorous state having a normal one-minute Apgar score (8-10). Fetal blood was obtained from the buttocks, or in some cases from the foot, at different sampling moments during labour from early first stage to immediately before delivery. Arterialized maternal capillary blood was sampled simultaneously at the different sampling moments. Sixteen obstetrically normal primiparae, all having normal labour and delivered of vigorous infants in the occiput anterior presentation, were a control series. Acid-base components, plasma lactate, pyruvate, and



glucose were determined in both groups; oxygen saturation only in the breech deliveries.

No major differences were found concerning the measured parameters in blood obtained from the fetal breech compared with blood from the fetal scalp in the first stage of labour; in addition, the composition of the fetal blood obtained from the breech in the terminal phase of labour was well related to that of the umbilical cord blood at birth. Consequently, fetal blood obtained from the breech or foot was, concerning acid-base and carbohydrate components, as representative for the blood of the main fetal circulation the fetal scalp blood.

Apart from these general statements, certain differences between vertex and breech presentation, concerning the biochemical features, were seen at the end of labour. In normal breech deliveries, fetal pH tended to decrease more than in the control series; this was correlated to a more marked rise in mean  $P_{CO_2}$ . This fetal pH drop resulted in an increased  $\Delta pH$  to about 0.20 pH units at the end of the second stage of labour compared with 0.13 pH units in the first stage, which may be interpreted as a biochemical warning sign suggesting a beginning of fetal metabolic acidosis. The findings, together with higher mean fetal plasma lactate and rise of  $BD_{ECF}$  noted at repeated determinations in the very last phase of labour in breech deliveries, suggest that this part of labour is more critical than in the vertex presentation.

In addition, three cases of breech deliveries were included in this study, where the infants at birth showed signs of fetal distress (Apgar score  $\leq 7$ ). All of them had biochemical disturbances in the blood obtained from the fetus before delivery in terms of increased maternal-fetal pH difference or negative maternal-fetal  $BD_{ECF}$  value.

#### Comments.

Blood taken from the breech or foot in breech or breech-foot deliveries was found to be as representative for the blood of the main fetal circulation as is fetal scalp blood in vertex deliveries. Consequently, the use of "fetal breech blood" would seem to be of the same clinical value as fetal scalp blood in assessing the fetal condition during labour.

Biochemical signs of fetal metabolic acidosis at the final few minutes of labour in breech presentation suggest the importance of making this part of delivery as short as possible, and to apply procedures facilitating this,

not only prophylactic episiotomy and release of arms, but also immediate use of forceps on aftercoming head on wide indications.

#### STUDIES ON THE CORRELATION BETWEEN CLINICAL SIGNS OF FETAL DISTRESS AND CHANGES IN FETAL AND MATERNAL METABOLISM DURING LABOUR. CONSIDERATIONS CONCERNING THE APPLICATION OF BIOCHEMICAL SUPERVISION OF THE FETUS IN THE CLINICAL ROUTINE (VI, VII)

The development of electronic FHR monitoring techniques and of biochemical determinations in fetal blood during labour has in a few years extended the scope of activity to be covered by the obstetrical clinician. Therefore his knowledge must include the new discipline prenatalology, "intrauterine pediatrics". The general adoption of those techniques in the clinical routine is as yet in a rather initial phase. In this country, this applies in particular to the biochemical supervision of the fetus. The hesitation shown by the clinicians in this respect is understandable in view of the interpretative problems still pertaining to data obtainable from fetal blood analyses, as exemplified by different standards laid down concerning the normal range and limits of the various blood components, and by different opinions regarding which components should be chosen for clinical use. The numerous factors that influence and disturb the correlation between data obtained at biochemical determination or FHR monitoring and the true conditions of the fetus, and that to a varying extent give rise to false normal and false abnormal groups of cases, were elucidated and analysed by James et al. (1968) and Bowe et al. (1970).

For clinical purposes, the main interest has been focused on fetal pH or fetal acid-base status. It has been stated (Saling 1962, Saling 1966, Bretscher & Saling 1967) that determination of fetal pH and pH<sub>qu40</sub> (i. e. standard bicarbonate) might provide sufficient information on the intrauterine condition of the fetus. However, in view of the intimate relation between the maternal and the fetal biochemistry, the maternal-fetal pH difference ( $\Delta$ pH) (Jacobson 1970, Vretos 1970, Khazin & Hon 1971 a + b, Rooth et al. 1973, Seidenschnur et al. 1973) and the maternal-fetal BD difference ( $\Delta$ BD) (Beard 1968, Vretos 1970, Roversi & Canussio 1970, Seidenschnur & Heinrich 1973) have been advanced as important indicators of the fetal oxygenation status. The value of determining fetal and maternal lactate and pyruvate and of the ratio between them (L/P ratio) has also been considered (cf. Schmidt & Bretscher 1970).

The motivation and aim of the present studies may be summarized as follows:

- 1) To contribute to the actual and important discussion, mentioned above, on the value of biochemical supervision of the fetus during labour and on the proper model of such a supervision, by studying - in series well defined on the basis of clinical signs of fetal distress - which biochemical metabolic changes are characteristic for the different signs. The study was therefore designed to cover not only acid-base variables, but also components of the carbohydrate and lipid metabolism in both fetal and maternal blood, sampled simultaneously.
- 2) To consider the results of such a systematic study in a Swedish material in relation to series published in other countries. The composition of obstetrical materials from different clinics, particularly from different countries, might vary widely. It would seem that, in this country, cases of very severe fetal distress are currently rare, most such cases being of moderate degree. This could give a different impression of the diagnostic situations encountered than might apply in other places that have a higher frequency of more severe conditions of fetal asphyxia.
- 3) A particular interest was focused on the  $\Delta\text{pH}$  and its significance in this study, adding to our previous studies reported (see references above). The clinical application of  $\Delta\text{pH}$  should give rise to certain considerations of a theoretical nature (separately dealt with in Paper VII).

#### A. The study on different signs of fetal distress (VI)

The series comprises delivery cases with different clinical signs of fetal distress during labour and infants presenting low Apgar score at birth. The groups are defined as follows:

Group A. Meconium-stained amniotic fluid with normal fetal heart rate (FHR) ( $n = 20$ ). Two infants had Apgar score  $\leq 7$ .

Group B. Meconium-stained amniotic fluid and fetal bradycardia ( $n = 20$ ). Five infants had Apgar score  $\leq 7$ .

Group C. Fetal bradycardia (non-stained amniotic fluid) ( $n = 16$ ). Two infants had Apgar score  $\leq 7$ .

Group D. Fetal tachycardia ( $n = 12$ ). Two infants had Apgar score  $\leq 7$ .

Group E. Low one minute Apgar score  $\leq 7$  ( $n = 14$ ). The Apgar score of the infants in this group was 4 in one, 5 in five, 6 in four, and 7 in four cases.

Group F. Normal controls ( $n = 19$ ).

Arterialized maternal blood and fetal scalp blood were obtained simultaneously, and the following parameters were determined: acid-base balance (pH,  $P_{CO_2}$ , and  $BD_{ECF}$ ) plasma lactate, pyruvate, glucose,  $\beta$ -hydroxybutyrate, and glycerol (occasionally also  $O_2$  saturation and plasma sodium). FHR and intrauterine pressure was recorded by a Roche Cardiocograph. The following results were obtained, and all assays are expressed as mean values:

Maternal pH was higher in the Groups A-E compared with the control Group, although statistically significant difference was only found between the control Group and Group C in first and second stage. Fetal pH in Group A and in the control Group was almost identical in the first stage of labour. In the remaining series, fetal pH was lower, the lowest value being found in Group E, differing significantly from the control Group. In the second stage, the pH levels in Groups A-E fell below the control Group, the lowest pH value being found in Groups C and E, these values differing significantly from the control Group. The pH-value of umbilical cord blood agreed with these findings.

Maternal-fetal pH-difference  $\geq 0.20$  pH units was related to the Groups B, C, and E in the second stage. Statistically, the frequency of pH values  $\geq 0.20$  was significantly higher in Group E than in the control Group. In the first stage of labour,  $\Delta pH \geq 0.20$  was found in Groups C-E. The frequency of  $\Delta pH$  values  $\geq 0.15$  pH units was found to be statistically higher in Groups B and C taken together both in the first and second stage of labour than in the control Group.

Maternal  $P_{CO_2}$  in Group C was significantly lower than in the control Group. Higher fetal  $P_{CO_2}$  values were found in the Groups A-E than in the control Group in the second stage.

Maternal and fetal  $BD_{ECF}$  values and maternal-fetal  $BD_{ECF}$  difference did not differ significantly between the groups.

Maternal plasma glucose was higher in Groups A-E in the first stage of labour than in the control Group, but no significant difference in fetal plasma glucose existed in Groups A-E compared with the control Group.

Both fetal and maternal plasma lactate increased during labour, the single lactate values covering a wide range in every group, primarily in the second stage. Only in the Groups C and E in the second stage and in umbilical arterial blood in these groups was fetal lactate significantly higher than in the control Group.



Plasma pyruvate increased during labour both in fetus and mother, and no significant differences were seen between the groups. However, the lactate/pyruvate ratios were higher in the Groups B-E, although no statistical differences were seen.

Maternal and fetal  $\beta$ -hydroxybutyrate usually increased in all Groups during labour.

Plasma glycerol rose both in mothers and in fetuses during labour in all Groups. The plasma glycerol concentration was significantly higher in the umbilical vein than in the artery.

### B. Theoretical aspects on maternal-fetal pH difference ( $\Delta$ pH)

The study is based on the theoretical argument of  $\Delta$ pH as expression of the maternal-fetal  $[H^+]$  ion difference,  $\Delta[H^+]$ , and deals with the problems that arise because pH is a logarithmical function. From a mathematically calculated nomogram for the relation between  $\Delta$ pH and  $\Delta[H^+]$  at different pH levels, it is concluded that pH might be misleading at very high maternal pH value and particularly at sudden changes from, for instance, high to low maternal pH. The practical relevance of this is illustrated by the results of a series of actual cases (hyperventilating mothers in the paracervical block series).

The importance of these theoretical aspects on  $\Delta$ pH, used in clinical practice, should primarily be considered at extremely high (or low) maternal pH-values. However, within the usually occurring pH limits, this aspect is of minor importance.

### Comments

As previously mentioned, the general feature in the investigation on different signs of fetal distress was that the infants of the series were only moderately asphyxiated.

Meconium-stained amniotic fluid was not usually correlated to biochemical disturbances. However, two depressed infants were found in the group. In these two delivery cases, an increased  $\Delta$ pH or low fetal pH, as signs of impaired oxygenation, was present during labour.

More depressed infants were seen in the group of meconium-stained amniotic fluid and fetal bradycardia than in the other bradycardia group having non-stained amniotic fluid. But the latter group showed more pro-

nounced biochemical changes. The two groups of bradycardia are composed of cases of base-line bradycardia or repeated late and variable decelerations, and it is uncertain whether the differences found between the groups express a true difference in view of the fact that the degree of bradycardia is difficult to define quantitatively. If the two groups are considered together, the acid-base changes were more marked, particularly concerning fetal pH and  $\Delta\text{pH}$  than if the groups are considered separately. However, an interesting finding was of significantly higher frequency of hyperventilating mothers in the group of fetal bradycardia with non-stained amniotic fluid than in the control group.

The type of fetal tachycardia in this series was increased base-line FHR. The group did not differ from the control group concerning the determined biochemical variables. In other words, fetal tachycardia of this kind showed no signs of influencing the fetal metabolism. But it should be noted from the literature, that fetal tachycardia in combination with deceleration pattern might be more correlated to biochemical disturbances.

In the low Apgar score group, many fetuses showed lowered pH and increased  $\Delta\text{pH}$  as a sign of impaired oxygen supply before birth. However, several cases showed normal biochemical status, supporting the view advanced by many authors that factors other than disturbed oxygen supply might cause depression of the infant at birth.

The study was further aimed at attempting the most informative and suitable parameter from a clinical point of view to discover impairment of the oxygen supply to the fetus. Among the great number of parameters assayed in this study, the fetal pH and maternal-fetal pH difference seems to be appropriately informative. As pointed out above, at very high or low maternal pH values, the limits for  $\Delta\text{pH}$  must be modified because of the logarithmical character of  $\Delta\text{pH}$  which is not expressing the maternal-fetal  $\text{H}^+$  ion difference linearly. In view of this and with the  $\Delta\text{pH} \geq 0.20$  pH units as upper limit for normal fetal condition, the result of the present study shows a low frequency of "false abnormals". Within the range of 0.15-0.19,  $\Delta\text{pH}$  is still, although to a lesser extent, correlated to fetal acidosis as a sign of fetal asphyxia.

## General summary

Fetal blood sampling and broad biochemical studies, including components of acid-base balance and of carbohydrate and lipid metabolism, were used to study the influence of different clinical and experimental conditions on the fetal and also on the maternal biochemistry.

### I-III.

- A. Double-blind technique was used to study the influence of paracervical block on mother and fetus ( $n = 60$ ). A very high frequency (50 %) of fetal bradycardia was found. Only moderate biochemical changes were seen. These were mainly bound to the acid-base parameters. Division of the material into bradycardia and non-bradycardia made it evident that the changes in acid-base balance were mainly bound to the bradycardia group. After pain relief, a rapid fall in maternal pH and a rise in  $P_{CO_2}$  were found, and the fetus showed the same changes. It was also found that the occurrence of fetal bradycardia was correlated to strong maternal hyperventilation before the block was applied. The results suggest possibilities for reducing the frequency of fetal bradycardia by postponing the paracervical block in strongly hyperventilating mothers until a normalization of the respiration has been induced by other means. Apart from single cases, no biochemical signs were found that suggest impairment of the oxygen supply to the fetus. This initiated the following series.
- B. Moderate ( $n = 19$ ) and severe ( $n = 12$ ) cases of fetal bradycardia after PCB were studied to further evaluate the influence of the paracervical block on the fetus. In the moderate bradycardia group, no significant biochemical signs of influenced fetal oxygenation were found. Contrary to this, parameters of acid-base balance and of carbohydrate and lipid metabolism (fetal pH, maternal-fetal pH difference, fetal plasma lactate, lactate/pyruvate ratio, and glycerol) were influenced, which suggests impaired oxygen supply to the fetus in connexion with severe fetal bradycardia. These biochemical findings, however, should be considered in relation to few depressed infants at birth, even in cases of severe bradycardia, which suggests that the fetuses were restored at birth.
- C. Determination of lidocaine concentration in fetal and maternal blood after paracervical block ( $n = 23$ ) and pudendal block ( $n = 18$ ) showed no difference between cases of fetal bradycardia and non-bradycardia, on one hand, and no substantial difference between paracervical block and pudendal block groups, on the other. The study further

supports the view that aetiological factors other than the height of the fetal blood concentration of local anaesthetics have to be considered in fetal bradycardia after paracervical block.

- IV. Since the role of the heart glycogen as an important factor for fetal survival during hypoxia was established in experimental animals, glucose infusion to the mother has widely been used. However, little is known about glucose load to humans. During normal labour, 13 parturients were given intravenous glucose infusion. Components of the carbohydrate and lipid metabolism and of acid-base balance, sodium, and haemoglobin were determined in maternal and fetal blood. Maternal insulin was assayed in 8 cases.

The maternal-fetal difference in plasma glucose increased with increasing maternal plasma glucose level. The glucose load caused a rapid early response of maternal insulin. No major disturbances of fetal acid-base balance were seen. The decrease of the initial  $\beta$ -hydroxybutyrate and glycerol concentration after glucose load suggested a negative caloric balance in normal labour patients. Fetal and maternal glycerol concentrations varied independently. Taken together with the observation made in some of the other series of the present investigation that fetal glycerol concentration tends to increase during normal labour, this suggests that fetal lipid mobilization occurs already antenatally. No changes in fetal and maternal water balance were induced by the hypertonic glucose infusion.

The study should be seen as a basic investigation on the clinical problem of advantages and disadvantages connected with maternal glucose infusion in order to ameliorate the fetal glycogen reserves.

- V. The application of fetal blood sampling in breech deliveries has attracted very little attention in the literature. Fetal and maternal acid-base balance and carbohydrate metabolism were studied in normal breech deliveries ( $n = 15$ ) and in a control series delivered in vertex presentation ( $n=16$ ). It was concluded that fetal blood obtained in breech presentation is as representative of the blood of the main fetal circulation as is the scalp blood. It was also shown that biochemical changes concerning different blood components in the very last minutes labour in breech deliveries suggest that this phase is critical for the fetus. Routines aimed at shortening this particular stage must be evolved. The use of "fetal breech blood" in attempting to evaluate the intrauterine condition of the fetus was exemplified by three cases with depressed infants at birth.



- VI- Classical signs of fetal distress were investigated in five groups;  
VII. A/ passage of meconium (n=20). B/ passage of meconium and  
fetal bradycardia (n=20). C/ fetal bradycardia (n=20). D/fetal  
tachycardia (n=12). E/ low one-minute Apgar score (n=14).  
Also 19 normal controls were investigated.

The most pronounced biochemical findings, compared with the control group, were seen in the two bradycardia groups and in the low Apgar score group. Apart from a few single cases, no influence on the fetal biochemistry was seen in the other two groups. The biochemical disturbances found were mainly related to acid-base parameters. It was concluded that information obtained from fetal pH and maternal-fetal pH difference ( $\Delta\text{pH}$ ) would seem adequate for clinical routine assessment of the intrauterine fetal condition. Certain additional considerations of theoretical nature on the  $\Delta\text{pH}$  concept are given in paper VII.

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A DOUBLE-BLIND STUDY OF THE INFLUENCE ON FETAL AND  
MATERNAL BIOCHEMISTRY OF PARACERVICAL BLOCK DURING LABOUR

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The first report on paracervical block anaesthesia in labour was given by Gellert in 1926. Presently, data on more than 70,000 instances of paracervical block are available in the literature (see reviews by Teramo, 1971; Thiery & Vroman 1972). Despite this amount of data, there are still, as pointed out by Thiery & Vroman, uncertainty and disparity of opinions concerning the possible hazards to the fetus of this method of obstetrical anaesthesia. This applies in particular to the most common side-effect of the anaesthesia, transient fetal bradycardia. Neither the factors predisposing to this fetal bradycardia, nor the influence of paracervical block on the fetal energy metabolism, are satisfactorily revealed. In fact, investigations on these basic problems related to paracervical block are rather limited in number and in the main restricted to acid-base measurements (see Teramo & Widholm 1967; Hickl & Kirchner 1968; Jung *et al.* 1969; Obolensky *et al.* 1969; Teramo 1969a & b; Asling *et al.* 1970; Busch & Lübbert 1970; Thiery *et al.* 1971; Teramo 1971; Vasicka *et al.* 1971). In addition to acid-base determinations, Frangipani *et al.* (1969) also measured maternal and fetal plasma lactate and pyruvate.

The present investigation was undertaken with the aim of analysing on a broad basis the influence of paracervical block on fetal and maternal metabolic blood components under defined experimental conditions. It was designed as a double-blind investigation, and the parameters chosen for determination concern acid-base balance, glucose, and lipid metabolism. A preliminary and partial report of the results of the investigation was previously given (Jacobson & Gårdmark 1972).

## MATERIAL AND METHODS

The material comprises 60 women aged 30 years or younger, all having an uncomplicated pregnancy. All were nulliparae, and the labour was in all respects normal at the time when the paracervical block was applied. A further prerequisite at the selection of cases was that the women experienced their labour as very painful.

The blocks were administered in the first stage of labour, at a cervical dilatation of 3-5 cm, and always by the same person and with the same technique. 20 ml solution was used, 10 ml being injected into each lateral fornix at 4 and 8 o'clock with a very short Kobak needle, giving an injection depth of 2-3 mm.

Four different solutions, codified according to ordinary double-blind technique, were used, and the series of women was divided into four groups of 15 patients. Group A received 20 ml 0.5% lidocaine (Xylocain<sup>®</sup>), equal to 100 mg lidocaine; Group B received 20 ml 0.5% lidocaine with epinephrine 1:400,000; Group C, 20 ml saline solution; Group D, 20 ml saline solution with epinephrine 1:400,000.

Fetal scalp blood and arterialized capillary blood from the fingertip of the mother were simultaneously sampled at three sampling periods:

- 1) 5 minutes before the paracervical injection; 2) 20 minutes after, and
- 3) 60 minutes after the injection.

At the three sampling periods, certain clinical factors were also recorded to evaluate the anaesthetic effect. These factors were: general muscular tension, general behaviour, audible reactions (cry etc.), frequency of respiration, pulse rate, and blood pressure of the mother. The fetal heart rate (FHR) was monitored by means of auscultation, being almost continuous during the first 20 minutes after the paracervical injection, and intermittent with short intervals between 20 and 60 minutes after the injection.

At each sampling, approximately 800  $\mu$ l of scalp blood was anaerobically collected by light suction into heparinized glass capillaries, about 20 cm in length. The maternal blood was sampled into short glass tubes, immediately sealed, for the determinations of pH and  $P_{CO_2}$ , and into small plastic tubes (adapted for the Beckman high speed micro-centrifuge) for determination of the remaining blood components.

The blood components determined were: pH,  $P_{CO_2}$ , base deficit ( $BD_{ECF}$ ), plasma glucose, lactate, pyruvate,  $\beta$ -hydroxybutyrate, and glycerol. pH was measured by means of the Radiometer micro-electrode and pH-meter PHM 27.  $P_{CO_2}$  was determined with the Eschweiler micro- $CO_2$ -electrode assembly. Base deficit for the extracellular fluid compartment was calculated from the Siggaard-Andersen alignment nomogram (1963), read at the Hb 5g/100 ml-line. The remaining components were determined by means of microadaptations of measuring methods commonly used. Plasma glucose was determined by means of the glucose oxidase method, described by Marks (1959); plasma lactate with the Boehringer enzymatic and spectrophotometric method, slightly modified (Boehringer Bulletin TC-B 1972; Rooth 1967); plasma pyruvate with an ultra-microadaptation of the Boehringer enzymatic method using spectrofluorometry for the final stage (Rooth 1967); plasma  $\beta$ -hydroxybutyrate by means of the  $\beta$ -hydroxybutyrate dehydrogenase method of Williamson *et al.* (1962) somewhat modified (Persson 1970); and plasma glycerol with an enzymatic fluorometric micro-method, devised by Laurell & Tibbling (1966).



## RESULTS

### I. ANAESTHETIC EFFECT

All patients in Group A experienced pain relief. In three of them, the relief was partial, and in the remaining 12, total. In Group B, 12 of the 15 patients reported pain relief, the relief being complete in 10 and good in two. In the control Groups C and D, three patients experienced a moderate pain relief. Normalization and/or disappearance of muscular tension, general pain-related behaviour, and audible reactions occurred in 60-80 % of those in Groups A and B. The frequency of respiration was normalized in 90 % of those in Group A, and in 70 % of those in Group B. In these two groups, a significant decrease in the maternal pulse rate was also noted 20 minutes after the block. In the Groups C and D, practically no changes were recorded after the paracervical injection concerning the clinical factors here mentioned. In all the groups, no changes in maternal blood pressure were registered. (For further details, refer to our previous report, Gårdmark *et al.* 1972.) The mean duration of the pain relief was 50 minutes in Group A and 90 minutes in Group B.

### II. EFFECTS ON LABOUR, FETAL HEART RATE, AND APGAR SCORE AT BIRTH

No significant differences between the groups were found concerning the progress of labour (cervical dilatation, descending of fetal head, frequency of uterine contractions) within an observation period of 90 minutes after the paracervical injection. Fetal bradycardia (i. e. FHR < 120 bpm) after the injection occurred in nine patients in Group A, and in six in Group B. In most of these fetal bradycardia cases, the FHR dropped below 100 bpm. In Group C, one instance of bradycardia was registered, but this patient had an extremely short duration of labour and the fetal bradycardia appeared immediately before delivery. In Group D, a slight lowering of the FHR to 118 bpm for about two minutes was noted after the injection in one patient. It follows that in the Groups A and B, receiving the active anaesthetic drug, 50 % of the cases developed transient fetal bradycardia.

In the Groups A and B, taken together, two infants had a one-minute Apgar score of 5, and two a one-minute score of 6-7. In the control Groups C and D, one had a one-minute Apgar score of 6. In the remaining cases of

all groups, the one-minute Apgar score was 8-10. The 5-minute Apgar score was 8-10 in all cases.

### III. BIOCHEMICAL RESULTS

#### a) The Groups A-D

pH (Table I, Figs. 1, 2, & 3). In the Groups A and B, a fall in the mean maternal and fetal pH values was found 20 minutes after the paracervical block. The decrease in the pH amounted to approximately 0.05 pH units in both maternal and fetal blood and equal in both groups. As seen from Fig. 2, the decrease was statistically significant for maternal as well as fetal pH. The statistical significance was highest for the maternal blood ( $p < 0.01$  in Group A, and  $p < 0.001$  in Group B). At 60 minutes after the block, the maternal and fetal mean pH level was significantly ( $p < 0.01$ ) raised and attained the initial level in Group A, whereas in Group B, the maternal and the fetal pH had increased to a value somewhat lower than the initial one. The maternal-fetal pH difference ( $\Delta$  pH) was almost constant around 0.13 pH units at all three sampling periods in the two groups.

In the Groups C and D, receiving paracervical injection with saline or saline with epinephrine, no changes were seen in the maternal and fetal pH mean values, except for a small but significant rise in the fetal pH 20 minutes after the block in Group C.

Pco<sub>2</sub> (Table I, Figs. 4, 5, & 6). The maternal Pco<sub>2</sub> mean value increased significantly during the first 20 minutes after the block in Group A ( $p < 0.05$ ) and Group B ( $p < 0.01$ ). The fetal Pco<sub>2</sub> mean value increased concomitantly in both groups, the increase being significant in Group A ( $p < 0.01$ ). At 60 minutes after the block, the mean Pco<sub>2</sub> of maternal and fetal blood was restored to the initial values in both groups.

In the control Groups C and D, the Pco<sub>2</sub> mean value remained almost constant throughout the observation period.

BD<sub>ECF</sub> (Table I, Figs. 7, 8, & 9). No statistically significant changes were seen in maternal and fetal BD<sub>ECF</sub> mean values in any of the groups A-D during the observation period. The fetal BD<sub>ECF</sub> values ranged

Mean pH in maternal and fetal blood 5 min. before (1), 20 min. after (2), and 60 min. after (3) PCB

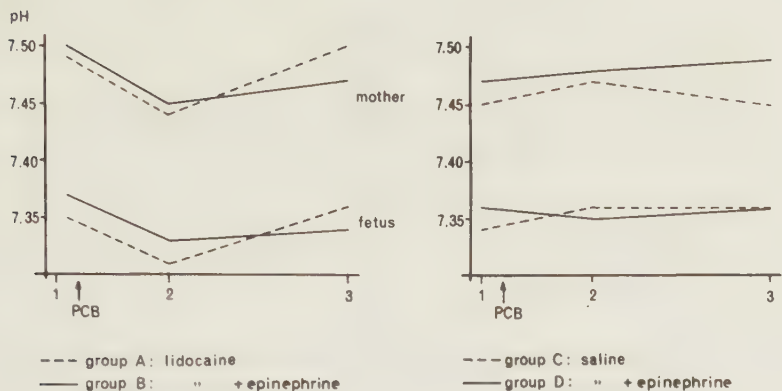


Fig 1. Mean pH in maternal and fetal blood at different sampling periods.

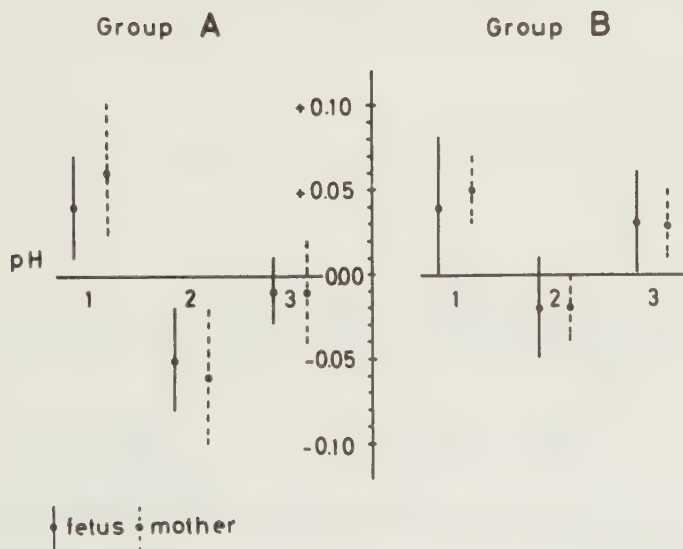


Fig 2. Mean fetal and maternal pH differences between the sampling periods in the groups A and B, and the 95 % confidence limits of the means.  
 1 = difference between sampling period 1 & 2;  
 2 = difference between sampling period 2 & 3;  
 3 = difference between sampling period 1 & 3.

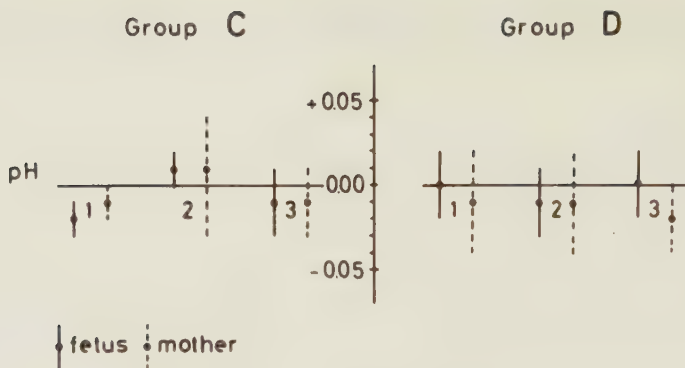


Fig 3. Mean fetal and maternal pH differences between the sampling periods in groups C and D, and the 95 % confidence limits of the means. See also legends of Fig 2.

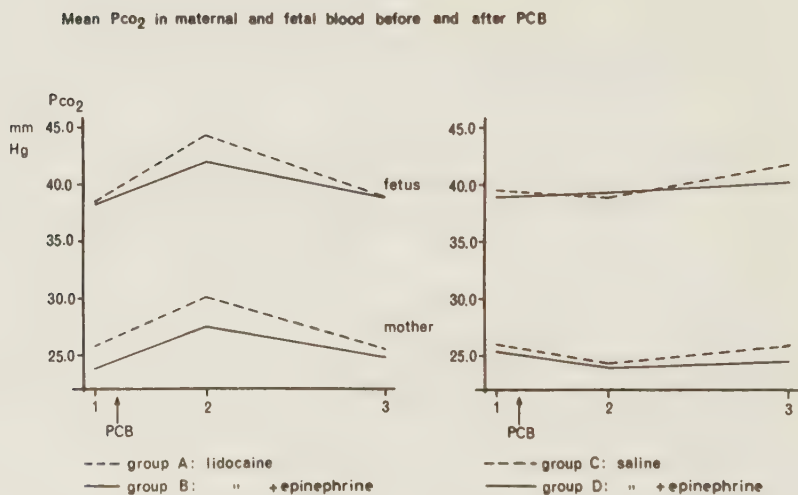


Fig 4. Mean  $P_{CO_2}$  in maternal and fetal blood at the different sampling periods.



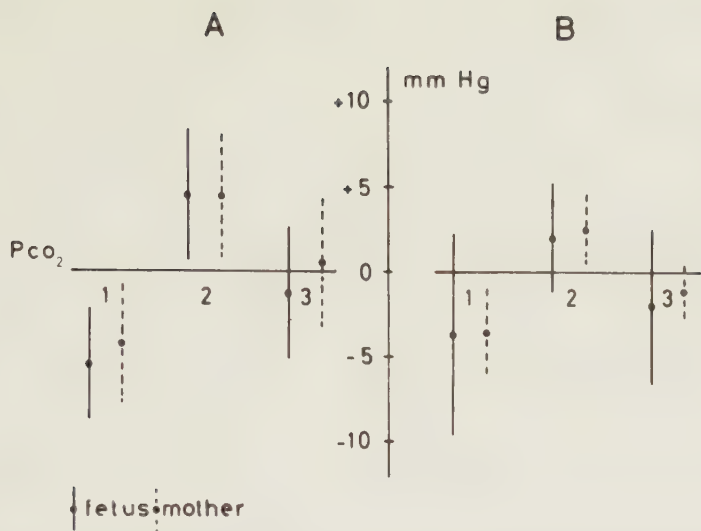


Fig 5. Mean fetal and maternal  $P_{CO_2}$  differences between the sampling periods in group A and B, and the 95 % confidence limits of the means. See also legends of Fig 2.

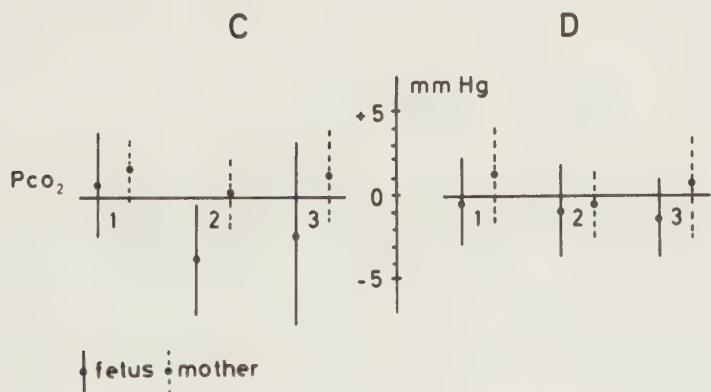


Fig 6. Mean fetal and maternal  $P_{CO_2}$  differences between the sampling periods in group C and D, and the 95 % confidence limits of the means. See also legends of Fig 2.

# Mean $BD_{ECF}$ in maternal and fetal blood before and after PCB

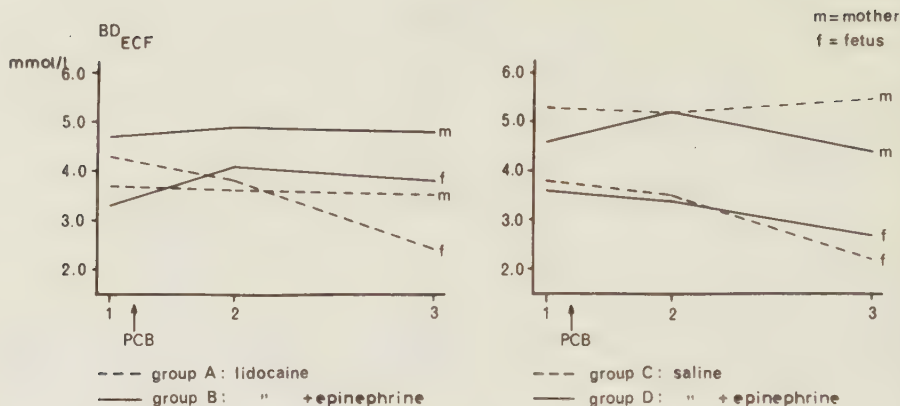


Fig 7. Mean  $BD_{ECF}$  in maternal and fetal blood at the different sampling periods.

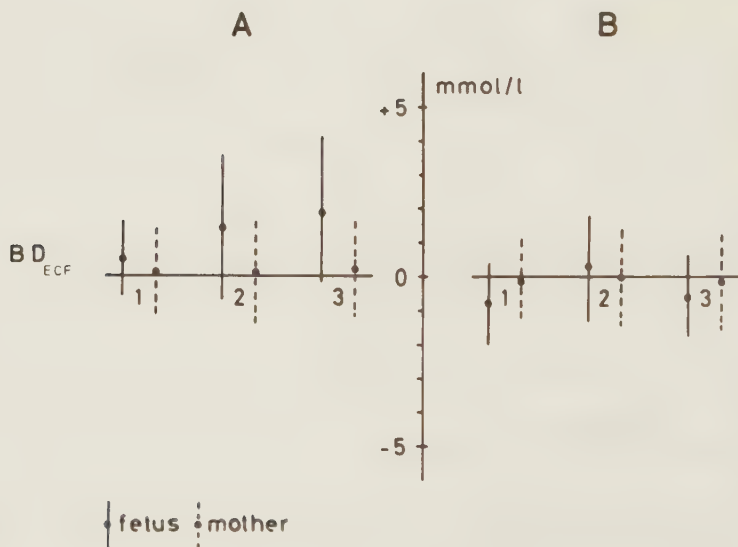


Fig 8. Mean fetal and maternal  $BD_{ECF}$  differences between the sampling periods in groups A and B, and the 95 % confidence limits of the means. See also legends of Fig 2.

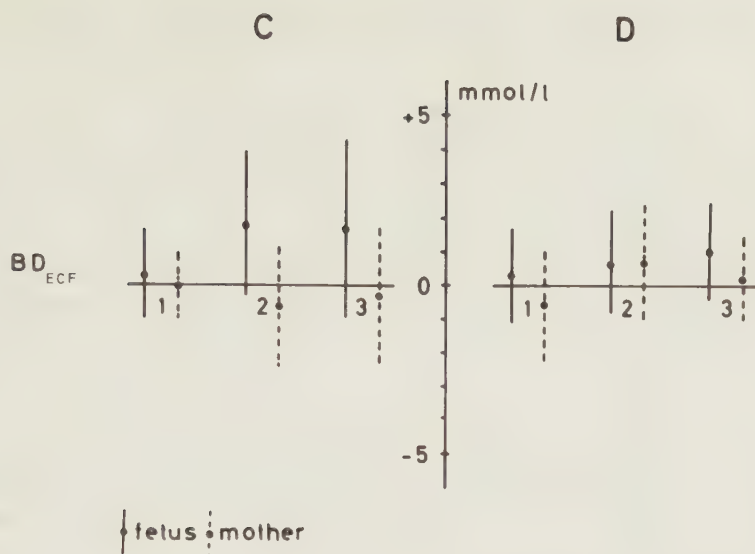


Fig 9. Mean fetal and maternal  $BD_{ECF}$  differences between the sampling periods in group C and D, and the 95 % confidence limits of the means. See also legends of Fig 2.

Table I. The mean value of the acid-base components and the 95 % conf. lim of the means.

|         |   | Before PCB    |                          |                             | 20 minutes after PCB |                          |                             | 60 minutes after PCB |                          |                             |
|---------|---|---------------|--------------------------|-----------------------------|----------------------|--------------------------|-----------------------------|----------------------|--------------------------|-----------------------------|
|         |   | pH            | Pco <sub>2</sub><br>mmHg | BD <sub>ECF</sub><br>mmol/l | pH                   | Pco <sub>2</sub><br>mmHg | BD <sub>ECF</sub><br>mmol/l | pH                   | Pco <sub>2</sub><br>mmHg | BD <sub>ECF</sub><br>mmol/l |
| Group A | M | 7.49<br>±0.03 | 25.8<br>±3.3             | 3.7<br>±1.3                 | 7.44<br>±0.01        | 30.1<br>±2.0             | 3.6<br>±1.4                 | 7.50<br>±0.04        | 25.6<br>±3.5             | 3.5<br>±1.4                 |
|         | F | 7.35<br>±0.03 | 38.6<br>±4.1             | 4.3<br>±2.1                 | 7.31<br>±0.08        | 44.3<br>±3.8             | 3.8<br>±2.3                 | 7.36<br>±0.03        | 39.9<br>±4.6             | 2.4<br>±1.9                 |
| Group B | M | 7.50<br>±0.03 | 23.8<br>±2.9             | 4.7<br>±1.5                 | 7.45<br>±0.03        | 27.5<br>±2.9             | 4.9<br>±1.0                 | 7.47<br>±0.03        | 24.9<br>±2.2             | 4.8<br>±1.3                 |
|         | F | 7.37<br>±0.02 | 38.2<br>±3.1             | 3.3<br>±1.6                 | 7.33<br>±0.30        | 42.0<br>±5.2             | 4.1<br>±1.9                 | 7.34<br>±0.02        | 39.9<br>±4.0             | 3.8<br>±1.7                 |
| Group C | M | 7.46<br>±0.03 | 26.0<br>±2.9             | 5.3<br>±1.7                 | 7.47<br>±0.03        | 24.4<br>±2.3             | 5.2<br>±1.6                 | 7.45<br>±0.03        | 25.9<br>±1.9             | 5.5<br>±1.6                 |
|         | F | 7.34<br>±0.01 | 39.5<br>±3.6             | 3.8<br>±1.7                 | 7.36<br>±0.02        | 38.9<br>±3.9             | 3.5<br>±2.0                 | 7.36<br>±0.03        | 41.8<br>±5.9             | 2.2<br>±2.5                 |
| Group D | M | 7.47<br>±0.03 | 25.4<br>±2.4             | 4.6<br>±1.7                 | 7.48<br>±0.03        | 24.1<br>±2.8             | 5.2<br>±1.8                 | 7.49<br>±0.04        | 24.6<br>±2.5             | 4.4<br>±1.4                 |
|         | F | 7.36<br>±0.02 | 38.9<br>±3.9             | 3.6<br>±1.7                 | 7.35<br>±0.02        | 39.3<br>±4.6             | 3.4<br>±2.1                 | 7.36<br>±0.03        | 40.3<br>±4.8             | 2.7<br>±2.2                 |

Table II. Means values of different components of the carbohydrate and lipid metabolism in maternal and fetal blood before and after PCB and the 95 % conf. lim. of the means.

|         |   | 5 minutes before PCB |             |               |               |                 | 20 minutes after PCB |             |               |               |                 | 60 minutes after |             |               |               |                 |
|---------|---|----------------------|-------------|---------------|---------------|-----------------|----------------------|-------------|---------------|---------------|-----------------|------------------|-------------|---------------|---------------|-----------------|
|         |   | Glucose              | Lactate     | Pyruvate      | $\beta$ -HB   | Glycerol        | Glucose              | Lactate     | Pyruvate      | $\beta$ -HB   | Glycerol        | Glucose          | Lactate     | Pyruvate      | $\beta$ -HB   | Glycerol        |
|         |   | mg%                  | m mol/l     | m mol/l       | m mol/l       | m mol/l         | mg%                  | m mol/l     | m mol/l       | m mol/l       | m mol/l         | mg%              | m mol/l     | m mol/l       | m mol/l       | m mol/l         |
| Group A | M | 108<br>±24           | 3.4<br>±1.1 | 0.16<br>±0.04 | 0.50<br>±0.22 | 0.175<br>±0.051 | 122<br>±23           | 2.4<br>±0.8 | 0.16<br>±0.05 | 0.48<br>±0.18 | 0.131<br>±0.035 | 127<br>±29       | 3.5<br>±1.1 | 0.18<br>±0.06 | 0.51<br>±0.20 | 0.207<br>±0.045 |
|         | F | 84<br>±17            | 4.1<br>±1.2 | 0.13<br>±0.03 | 0.16<br>±0.05 | 0.068<br>±0.017 | 94<br>±18            | 4.6<br>±1.3 | 0.15<br>±0.07 | 0.20<br>±0.07 | 0.072<br>±0.026 | 86<br>±13        | 4.4<br>±1.5 | 0.13<br>±0.04 | 0.21<br>±0.10 | 0.092<br>±0.025 |
| Group B | M | 117<br>±18           | 2.8<br>±0.6 | 0.14<br>±0.04 | 0.87<br>±0.36 | 0.245<br>±0.102 | 125<br>±22           | 2.7<br>±0.5 | 0.14<br>±0.04 | 1.03<br>±0.32 | 0.149<br>±0.030 | 110<br>±16       | 2.7<br>±0.6 | 0.17<br>±0.05 | 0.73<br>±0.33 | 0.163<br>±0.043 |
|         | F | 75<br>±8             | 3.1<br>±0.8 | 0.08<br>±0.02 | 0.25<br>±0.24 | 0.076<br>±0.021 | 87<br>±13            | 4.7<br>±1.6 | 0.14<br>±0.05 | 0.37<br>±0.12 | 0.081<br>±0.021 | 84<br>±12        | 4.5<br>±1.5 | 0.13<br>±0.03 | 0.28<br>±0.09 | 0.101<br>±0.054 |
| Group C | M | 105<br>±18           | 2.7<br>±0.7 | 0.13<br>±0.02 | 0.77<br>±0.27 | 0.190<br>±0.052 | 104<br>±14           | 3.1<br>±0.9 | 0.16<br>±0.05 | 0.86<br>±0.24 | 0.174<br>±0.030 | 122<br>±18       | 3.2<br>±0.8 | 0.15<br>±0.05 | 0.82<br>±0.39 | 0.174<br>±0.049 |
|         | F | 81<br>±11            | 3.6<br>±0.7 | 0.12<br>±0.03 | 0.25<br>±0.18 | 0.057<br>±0.012 | 73<br>±9             | 3.9<br>±0.8 | 0.12<br>±0.03 | 0.32<br>±0.20 | 0.083<br>±0.029 | 93<br>±16        | 3.8<br>±0.8 | 0.15<br>±0.04 | 0.35<br>±0.24 | 0.066<br>±0.030 |
| Group D | M | 101<br>±17           | 4.1<br>±2.0 | 0.17<br>±0.05 | 0.61<br>±0.23 | 0.204<br>±0.036 | 115<br>±28           | 3.3<br>±0.5 | 0.19<br>±0.04 | 0.77<br>±0.26 | 0.168<br>±0.042 | 107<br>±20       | 3.5<br>±0.9 | 0.17<br>±0.05 | 0.75<br>±0.25 | 0.205<br>±0.038 |
|         | F | 81<br>±14            | 3.7<br>±1.1 | 0.12<br>±0.03 | 0.34<br>±0.19 | 0.069<br>±0.015 | 83<br>±12            | 4.8<br>±1.4 | 0.15<br>±0.03 | 0.22<br>±0.07 | 0.075<br>±0.023 | 92<br>±15        | 4.8<br>±1.8 | 0.14<br>±0.04 | 0.22<br>±0.07 | 0.075<br>±0.018 |



between 2 and 4 mmol/l, and the maternal BD<sub>ECF</sub> values ranged between 3 and 5 mmol/l.

Plasma glucose (Table II). In the Groups A and B, the fetal plasma glucose increased with approximately 10 mg% during the first 20 minutes after the block, the increase being statistically significant ( $p < 0.05$ ). An increase in the maternal plasma glucose concentration of about the same magnitude simultaneously occurred, although this increase was not statistically significant. In the Groups C and D, no statistically significant changes in the mean values of maternal and fetal plasma glucose concentration were found to occur.

Plasma lactate (Table II). On the whole, the maternal and fetal plasma lactate values changed very little during the observation period in all the groups. In Group A, a small but significant ( $p < 0.05$ ) decrease in the maternal plasma lactate mean value was seen during the first 20 minutes after the block, and in Group B, the mean concentration of the fetal plasma lactate increased significantly ( $p < 0.05$ ) during the same period. In Group C, no significant changes occurred, but in Group D, the fetal plasma lactate mean value increased with approximately 1 mmol/l during the first 20 minutes after the block ( $p < 0.05$ ).

Plasma pyruvate (Table II). The maternal and fetal plasma pyruvate concentration also showed very small changes during the observation period, the only noticeable change being a moderate increase in the fetal pyruvate mean value during the first 20 minutes after the block ( $p < 0.05$ ) in Group B.

Plasma  $\beta$ -hydroxybutyrate ( $\beta$ -HB) (Table II). The maternal plasma  $\beta$ -hydroxybutyrate mean concentration change in all the groups was small but tended to increase after the block. The fetal plasma  $\beta$ -hydroxybutyrate mean values also tended to increase, the increase during the first 20 minutes being significant in Group A ( $p < 0.05$ ) and in Groups B and C ( $p < 0.01$ ).

Plasma glycerol (Table II). In all groups, the maternal mean concentration of plasma glycerol decreased during the first 20 minutes after the paracervical injection, the decrease being statistically significant only in Group A ( $p < 0.05$ ). Between 20 and 60 minutes after the block, the maternal glycerol level tended to rise again. Contrary to the maternal

changes, the fetal plasma glycerol mean concentration tended to increase during the first 20 minutes after the injection, but not to a statistically significant degree. In the Groups A and B, the increase continued between the 20 and 60 minute sampling periods. The total increase in the fetal plasma glycerol mean value was significant in Group A ( $p < 0.05$ ).

b) The Groups A and B, divided into bradycardia ( $n = 15$ ) and non-bradycardia ( $n = 15$ ).

pH (Table III, Figs. 10 & 11). The maternal pH mean value was higher immediately before the paracervical block in the bradycardia group than in the non-bradycardia group (7.51 versus 7.47), the difference being significant ( $p < 0.05$ ). During the first 20 minutes after the block, the maternal pH mean value showed a highly significant fall in the bradycardia group ( $p < 0.001$ ). At 60 minutes after the block, the maternal pH mean had returned to the initial level. Concomitantly with the maternal pH changes, the fetal pH mean value decreased significantly ( $p < 0.01$ ) in the first 20 minutes, and then rose again to the initial value in the bradycardia group. The maternal-fetal pH difference ( $\Delta$ pH) was approximately 0.15 pH units throughout the observation time in this group. In the non-bradycardia group, the maternal and fetal pH mean values showed a slight tendency to decrease during the first 20 minutes after the block, but the changes were statistically non-significant. The  $\Delta$ pH mean value was constantly around 0.10 pH units at all the sampling periods.

Pco<sub>2</sub> (Table III, Figs. 12 & 13). The initial mean value of the maternal Pco<sub>2</sub>, immediately before the block, was significantly lower in the bradycardia group than in the non-bradycardia group ( $p < 0.01$ ). The initial fetal Pco<sub>2</sub> values differed between the two groups in a similar way, although the difference was statistically non-significant. At 20 minutes after the block, the maternal Pco<sub>2</sub> mean value was significantly increased ( $p < 0.001$ ), as was the fetal Pco<sub>2</sub> mean value ( $p < 0.01$ ) in the bradycardia group. Between the 20- and 60-minute sampling periods, the maternal, as well as the fetal, Pco<sub>2</sub> mean values again decreased to levels not differing significantly from the initial ones.

In the non-bradycardia group, no significant changes, in either the maternal or the fetal Pco<sub>2</sub> mean values, were encountered during the observation period.

BD<sub>ECF</sub> (Table III, Figs. 14 & 15). The maternal BD<sub>ECF</sub> mean value remained constant throughout the observation period in both groups; these

Mean pH in the bradycardia and non-bradycardia group.

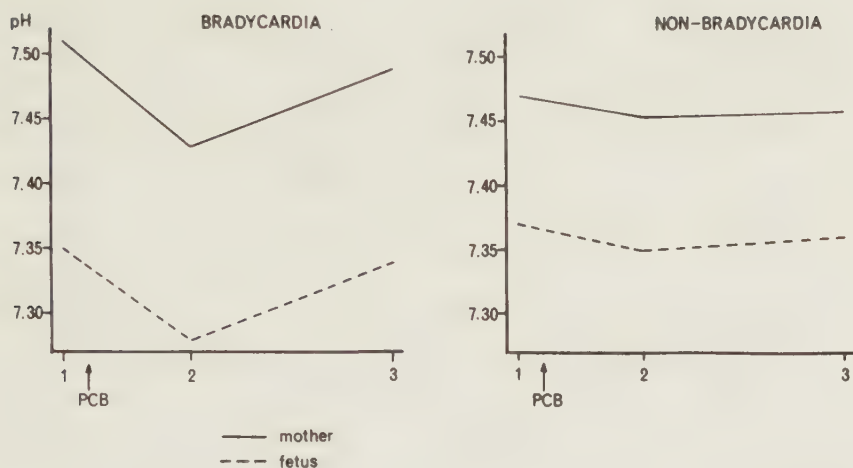


Fig 10. Maternal and fetal mean pH at the different sampling periods in the bradycardia and non-bradycardia groups.

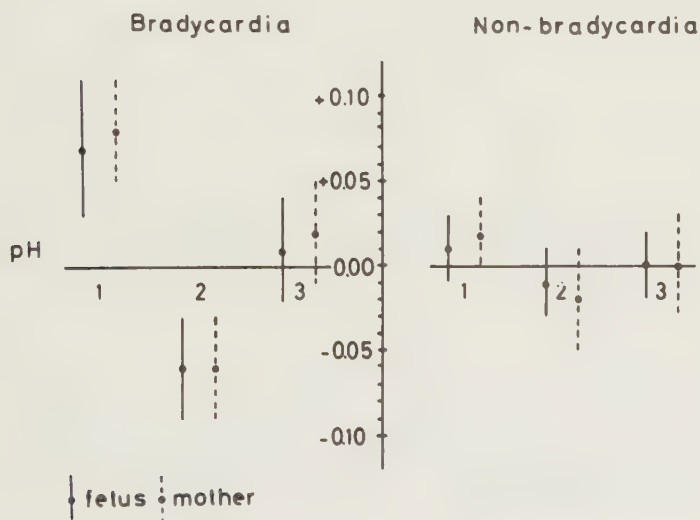


Fig 11. Mean fetal and maternal pH differences between the sampling periods in the bradycardia and non-bradycardia groups, and 95 % confidence limits of the means. See also legends of Fig 2.

# Mean $P_{CO_2}$ in the bradycardia and non-bradycardia group

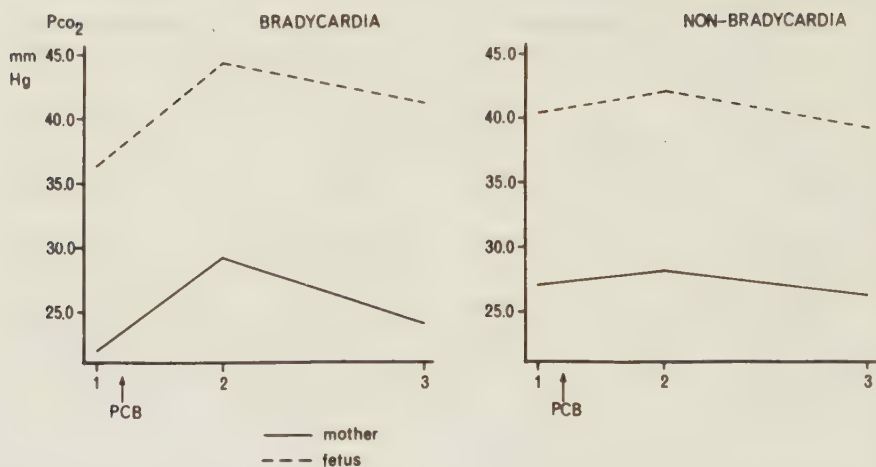


Fig 12. Maternal and fetal mean  $P_{CO_2}$  at the different sampling periods in the different sampling periods in the bradycardia and non-bradycardia groups.

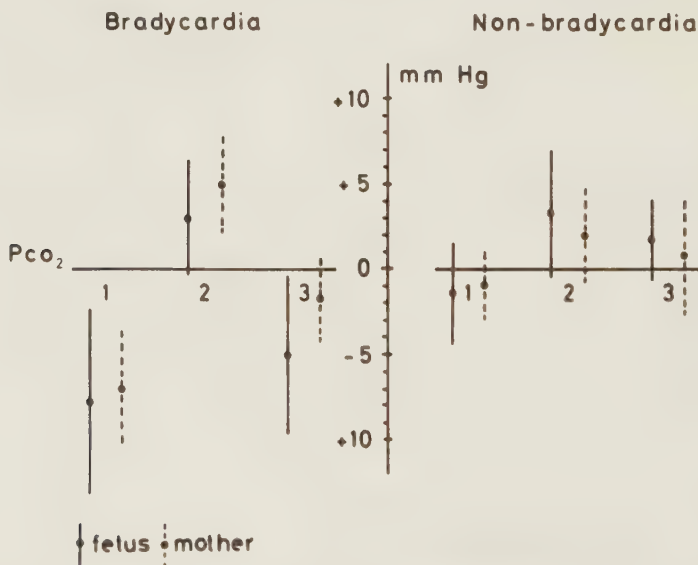


Fig 13. Mean fetal and maternal  $P_{CO_2}$  differences between the sampling periods in the bradycardia and non-bradycardia groups, and the 95% confidence limits of the means. See also legends of Fig 2.

Mean  $BD_{ECF}$  in the bradycardia and non-bradycardia group

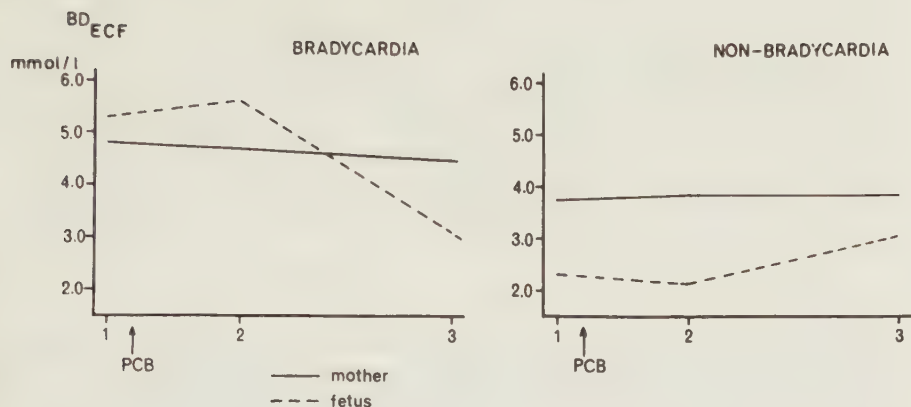


Fig 14. Maternal and fetal mean  $BD_{ECF}$  at the different sampling periods in the bradycardia and non-bradycardia groups.

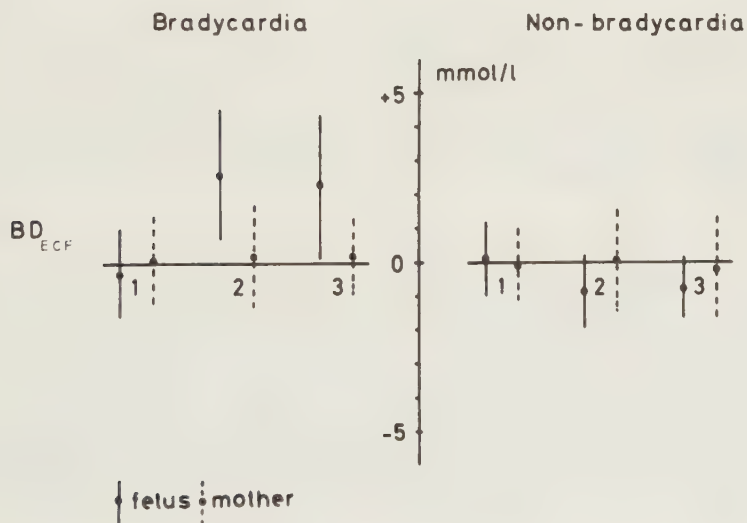


Fig 15. Mean fetal and maternal  $BD_{ECF}$  differences between the sampling periods in the bradycardia and non-bradycardia groups, and the 95 % confidence limits of the means. See also legends of Fig 2.



values did not differ between the two groups. In the bradycardia group, the initial mean value of the fetal  $BD_{ECF}$  was somewhat higher than the corresponding value in the non-bradycardia group ( $p < 0.05$ ) and exceeded slightly the maternal  $BD_{ECF}$ . After the paracervical block, however, the fetal  $BD_{ECF}$  mean in the former group decreased significantly between the 20- and 60-minute sampling periods ( $p < 0.05$ ), and at the end of the observation period, no significant difference between the groups was present concerning the fetal  $BD_{ECF}$  mean value. But it should be noted that in a few individual instances, a moderate increase in the fetal  $BD_{ECF}$  was found during the first 20 minutes after the block. The most pronounced of these is illustrated in Fig. 21.

Plasma glucose (Table IV, Fig. 16). The initial mean values of maternal and fetal plasma glucose concentration were somewhat lower in the bradycardia group than in the non-bradycardia group. During the first 20 minutes after the block, both the maternal and the fetal mean values of plasma glucose were significantly increased ( $p_m < 0.05$ , and  $p_f < 0.01$ ) in the bradycardia group and exceeded the corresponding mean values in the non-bradycardia group in which no changes in the maternal or fetal plasma glucose concentration occurred. In both groups, the fetal plasma glucose level was throughout lower than the maternal level.

Plasma lactate (Table IV, Fig. 17). Except for a moderate and significant increase in the mean fetal plasma lactate concentration ( $p < 0.05$ ) during the first 20 minutes after the block in the bradycardia group, both the maternal and the fetal plasma lactate mean values showed only small and non-significant variation.

Plasma pyruvate (Table IV, Fig. 18). The maternal plasma pyruvate mean concentration showed only small and statistically non-significant changes in both groups during the observation period. The fetal plasma pyruvate mean value increased significantly ( $p < 0.01$ ) by 0.08 mmol/l during the first 20 minutes after the paracervical block in the bradycardia group, and then decreased again almost to the initial value between the 20- and 60-minute sampling periods. No significant changes were seen in the non-bradycardia group concerning the fetal plasma pyruvate mean concentration.

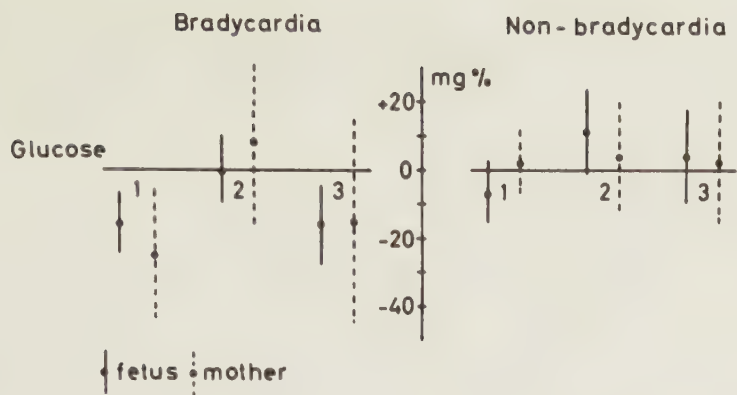


Fig 16. Mean differences of fetal and maternal plasma glucose concentration between the sampling periods in the bradycardia and non-bradycardia groups, and the 95 % confidence limits of the means. See also legends of Fig 2.

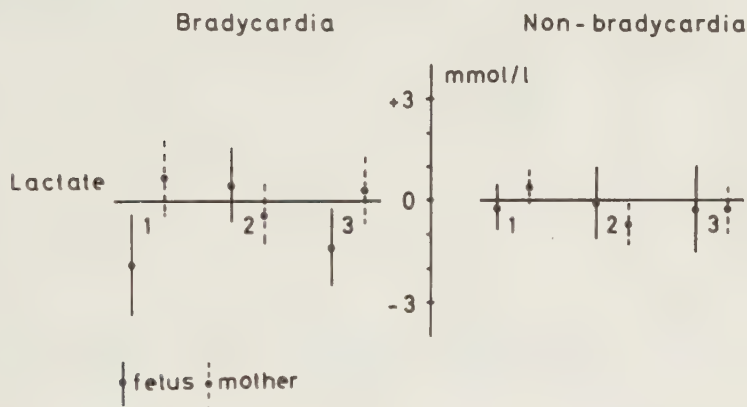


Fig 17. Mean differences of fetal and maternal plasma lactate concentration between the sampling periods in the bradycardia and non-bradycardia groups, and the 95 % confidence limits of the means. See also of Fig 2.

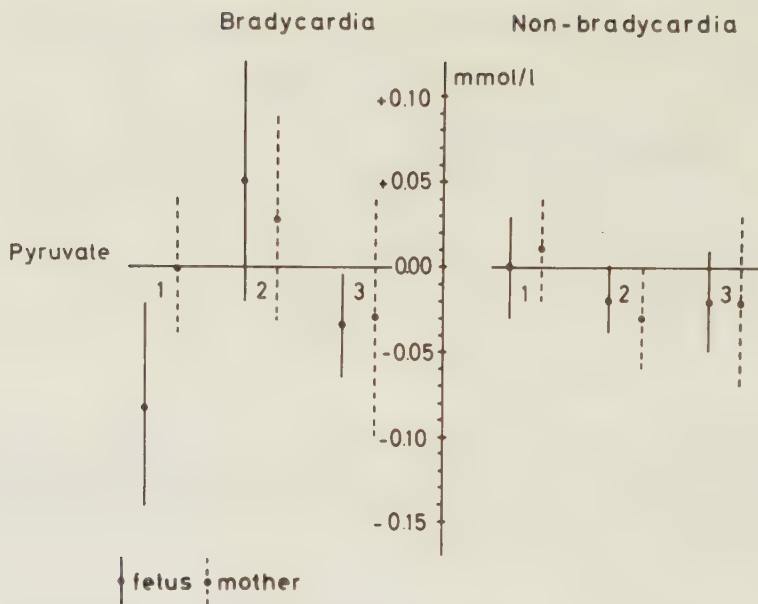


Fig 18. Mean difference of fetal and maternal plasma pyruvate concentration between the sampling periods in the bradycardia and non-bradycardia groups. See also legend of Fig 2.

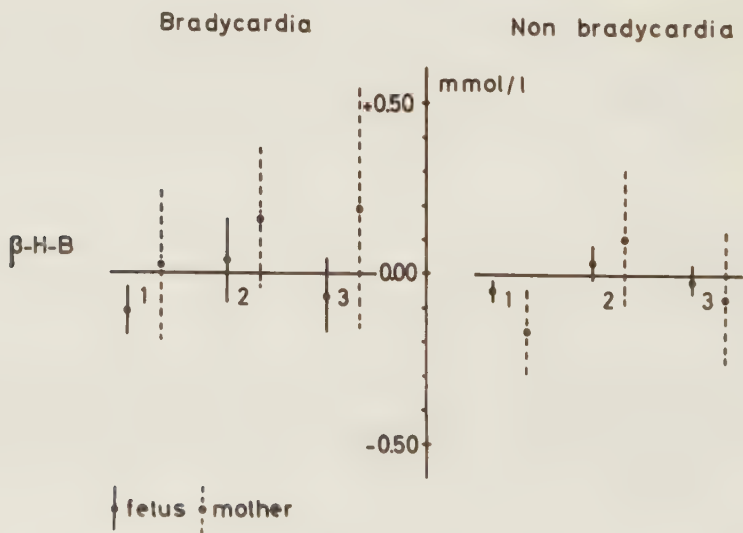


Fig 19. Mean differences of fetal and maternal plasma  $\beta$ -hydroxybutyrate concentration between the sampling periods in the bradycardia and non-bradycardia groups. See also legends of Fig 2.

Table III. Different maternal (M) and fetal (F) acid-base components in the bradycardia and non-bradycardia groups.

Mean values, standard deviations and 95 % confidence limits of the means.

|                             |   | Bradycardia |                  |      | Non-Bradycardia |                  |      |                  |
|-----------------------------|---|-------------|------------------|------|-----------------|------------------|------|------------------|
|                             |   | $\bar{x}$   | $\pm 95\%$ c lim | sd   | $\bar{x}$       | $\pm 95\%$ c lim | sd   |                  |
| PH                          | M | 7.51        | $\pm 0.03$       | 0.05 | 7.47            | $\pm 0.03$       | 0.05 | 5 min before PCB |
|                             | F | 7.35        | $\pm 0.03$       | 0.05 | 7.37            | $\pm 0.02$       | 0.04 |                  |
| Pco <sub>2</sub><br>mm Hg   | M | 22.3        | $\pm 2.5$        | 4.4  | 27.4            | $\pm 3.1$        | 5.6  |                  |
|                             | F | 36.3        | $\pm 3.0$        | 5.5  | 40.5            | $\pm 3.9$        | 6.8  |                  |
| BD <sub>ECF</sub><br>mmol/l | M | 4.7         | $\pm 1.1$        | 2.1  | 3.7             | $\pm 1.6$        | 2.9  |                  |
|                             | F | 5.3         | $\pm 1.7$        | 3.1  | 2.3             | $\pm 1.7$        | 3.0  |                  |
|                             |   |             |                  |      |                 |                  |      |                  |
| PH                          | M | 7.43        | $\pm 0.01$       | 0.01 | 7.46            | $\pm 0.03$       | 0.06 | 20 min after PCB |
|                             | F | 7.28        | $\pm 0.03$       | 0.05 | 7.35            | $\pm 0.02$       | 0.04 |                  |
| Pco <sub>2</sub><br>mm Hg   | M | 29.3        | $\pm 1.9$        | 3.4  | 28.4            | $\pm 3.2$        | 5.7  |                  |
|                             | F | 44.3        | $\pm 5.1$        | 9.2  | 42.0            | $\pm 4.0$        | 7.3  |                  |
| BD <sub>ECF</sub><br>mmol/l | M | 4.7         | $\pm 1.1$        | 1.8  | 3.8             | $\pm 1.4$        | 2.6  |                  |
|                             | F | 5.6         | $\pm 2.1$        | 3.8  | 2.2             | $\pm 1.6$        | 2.8  |                  |
|                             |   |             |                  |      |                 |                  |      |                  |
| PH                          | M | 7.49        | $\pm 0.03$       | 0.05 | 7.47            | $\pm 0.04$       | 0.07 | 60 min after PCB |
|                             | F | 7.34        | $\pm 0.02$       | 0.04 | 7.36            | $\pm 0.02$       | 0.04 |                  |
| Pco <sub>2</sub><br>mm Hg   | M | 24.0        | $\pm 2.4$        | 4.3  | 26.4            | $\pm 3.2$        | 5.8  |                  |
|                             | F | 41.2        | $\pm 4.2$        | 7.6  | 38.6            | $\pm 4.3$        | 7.7  |                  |
| BD <sub>ECF</sub><br>mmol/l | M | 4.5         | $\pm 1.5$        | 2.6  | 3.8             | $\pm 1.3$        | 2.3  |                  |
|                             | F | 3.0         | $\pm 1.9$        | 3.5  | 3.1             | $\pm 1.7$        | 3.0  |                  |

Table IV. Different maternal (M) and fetal (F) blood components of the carbohydrate and fat metabolism in the bradycardia and non-bradycardia groups.

Mean values, standard deviations and 95 % confidence limits of the means.

|                       |   | Bradycardia |                  |       | Non-Bradycardia |                  |       |  |
|-----------------------|---|-------------|------------------|-------|-----------------|------------------|-------|--|
|                       |   | $\bar{x}$   | $\pm 95\%$ c lim | sd    | $\bar{x}$       | $\pm 95\%$ c lim | sd    |  |
| Glucose<br>mg%        | M | 104         | $\pm 25$         | 40.7  | 120             | $\pm 16$         | 27.9  |  |
|                       | F | 78          | $\pm 12$         | 19.2  | 81              | $\pm 14$         | 24.2  |  |
| Lactate<br>mmol/l     | M | 3.5         | $\pm 1.0$        | 1.7   | 2.7             | $\pm 0.7$        | 1.2   |  |
|                       | F | 4.0         | $\pm 1.2$        | 2.1   | 3.1             | $\pm 0.8$        | 1.4   |  |
| Pyruvate<br>mmol/l    | M | 0.17        | $\pm 0.04$       | 0.08  | 0.14            | $\pm 0.04$       | 0.06  |  |
|                       | F | 0.12        | $\pm 0.03$       | 0.05  | 0.09            | $\pm 0.02$       | 0.05  |  |
| $\beta$ -HB<br>mmol/l | M | 0.70        | $\pm 0.31$       | 0.54  | 0.68            | $\pm 0.33$       | 0.57  |  |
|                       | F | 0.19        | $\pm 0.06$       | 0.11  | 0.22            | $\pm 0.10$       | 0.17  |  |
| Glycerol<br>mmol/l    | M | 0.205       | $\pm 0.042$      | 0.071 | 0.214           | $\pm 0.110$      | 0.182 |  |
|                       | F | 0.076       | $\pm 0.022$      | 0.035 | 0.067           | $\pm 0.016$      | 0.028 |  |
|                       |   |             |                  |       |                 |                  |       |  |
| Glucose<br>mg%        | M | 129         | $\pm 23$         | 35.5  | 118             | $\pm 21$         | 34.8  |  |
|                       | F | 93          | $\pm 16$         | 25.9  | 88              | $\pm 15$         | 26.5  |  |
| Lactate<br>mmol/l     | M | 2.8         | $\pm 0.8$        | 1.4   | 2.3             | $\pm 0.5$        | 1.0   |  |
|                       | F | 6.1         | $\pm 1.6$        | 2.7   | 3.3             | $\pm 0.7$        | 1.2   |  |
| Pyruvate<br>mmol/l    | M | 0.17        | $\pm 0.04$       | 0.09  | 0.13            | $\pm 0.04$       | 0.06  |  |
|                       | F | 0.20        | $\pm 0.07$       | 0.12  | 0.09            | $\pm 0.02$       | 0.04  |  |
| $\beta$ -HB<br>mmol/l | M | 0.68        | $\pm 0.17$       | 0.29  | 0.83            | $\pm 0.40$       | 0.69  |  |
|                       | F | 0.29        | $\pm 0.10$       | 0.18  | 0.27            | $\pm 0.12$       | 0.21  |  |
| Glycerol<br>mmol/l    | M | 0.159       | $\pm 0.031$      | 0.052 | 0.121           | $\pm 0.029$      | 0.045 |  |
|                       | F | 0.089       | $\pm 0.028$      | 0.045 | 0.066           | $\pm 0.015$      | 0.026 |  |
|                       |   |             |                  |       |                 |                  |       |  |
| Glucose<br>mg%        | M | 119         | $\pm 21$         | 35.1  | 118             | $\pm 25$         | 43.1  |  |
|                       | F | 94          | $\pm 15$         | 25.4  | 77              | $\pm 7$          | 11.4  |  |
| Lactate<br>mmol/l     | M | 3.2         | $\pm 1.0$        | 1.7   | 3.0             | $\pm 0.9$        | 1.5   |  |
|                       | F | 5.5         | $\pm 1.6$        | 2.8   | 3.4             | $\pm 1.1$        | 1.9   |  |
| Pyruvate<br>mmol/l    | M | 0.20        | $\pm 0.06$       | 0.11  | 0.16            | $\pm 0.04$       | 0.07  |  |
|                       | F | 0.15        | $\pm 0.04$       | 0.07  | 0.11            | $\pm 0.02$       | 0.04  |  |
| $\beta$ -HB<br>mmol/l | M | 0.51        | $\pm 0.19$       | 0.32  | 0.73            | $\pm 0.34$       | 0.60  |  |
|                       | F | 0.25        | $\pm 0.11$       | 0.19  | 0.24            | $\pm 0.09$       | 0.15  |  |
| Glycerol<br>mmol/l    | M | 0.186       | $\pm 0.047$      | 0.079 | 0.185           | $\pm 0.045$      | 0.074 |  |
|                       | F | 0.095       | $\pm 0.025$      | 0.042 | 0.098           | $\pm 0.054$      | 0.090 |  |

5 min before PCB

20 min after PCB

60 min after PCB



Plasma  $\beta$ -hydroxybutyrate ( $\beta$ -HB) (Table IV, Fig. 19). In the bradycardia group, the maternal plasma  $\beta$ -hydroxybutyrate mean concentration showed a small but constant tendency to decrease during the observation period, the decrease being statistically non-significant. The fetal mean value of plasma  $\beta$ -hydroxybutyrate showed a small but significant increase ( $p < 0.01$ ) during the first 20-minute period after the block in both groups, and after that a slight decreasing tendency.

Plasma glycerol (Table IV, Fig. 20). In both groups, the maternal plasma glycerol mean concentration tended to decrease during the first 20 minutes after the block, and then increase again during the 20-60 minute period. The decrease seen in the bradycardia group was statistically significant ( $p < 0.01$ ). The fetal plasma glycerol mean values showed in the bradycardia group a steady although moderate tendency to increase throughout the observation period, the fetal changes being statistically non-significant, however, as were also the fetal plasma glycerol changes in the non-bradycardia group.

## DISCUSSION

A marked feature in the present double-blind investigation was the high incidence of transient fetal bradycardia (50 per cent) encountered in the two groups of patients who received the active anaesthetic agent. The frequency figures usually reported vary between 1 and 30 per cent, although figures between 30 and 69 per cent exceptionally are reported (Teramo & Widholm 1967; Asling *et al.* 1970; Busch & Lübbert 1970; Teramo 1969, 1971). However, in view of the low dose of lidocaine used in the present study, and in view of the fact that the paracervical injection was applied at a very low depth, not exceeding 3 mm under the vaginal mucosa (cf. Hökegård 1972), the percentage of fetal bradycardia obtained is unexpectedly high. As a consequence of this, the present series will offer particularly good opportunities for studying fetal and maternal metabolic changes related to this kind of fetal bradycardia.

The most distinct differences found between the groups of patients receiving the anaesthetic drug and the control groups receiving saline or saline with epinephrine concern the  $P_{CO_2}$  and pH changes. It was primarily found that in the whole series the maternal  $P_{CO_2}$  mean value immediately before the block was low, amounting to 24-25 mm Hg, which is somewhat lower than is usually found at this stage of labour. The maternal pH mean value

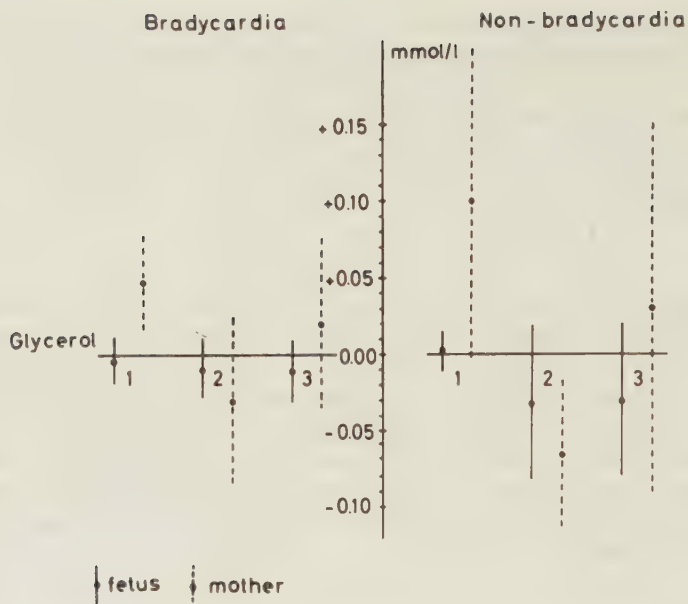


Fig 20. Mean differences of fetal and maternal plasma glycerol concentration between the sampling periods in the bradycardia and non-bradycardia groups. See also legends of Fig 2.

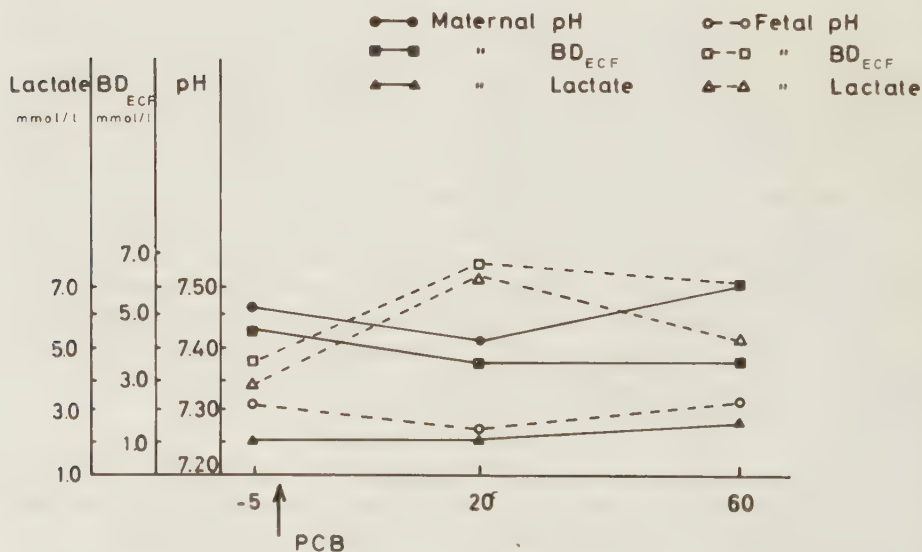


Fig 21. Maternal and fetal pH,  $BD_{ECF}$ , and plasma lactate values before and after paracervical anaesthesia in one case in Group A.

was at the same time high, approximately 7.50, the low  $P_{CO_2}$  thus being not fully compensated by the mean base deficit value of 4-5 mmol/l. The figures indicate that the mothers of this series were obviously hyperventilating at the time of the paracervical injection which is reasonable, as only patients with strong experience of pain were chosen for the study.

However, during the first 20 minutes after the injection, a marked increase in the maternal  $P_{CO_2}$  and a related fall in the maternal pH occurred in the groups given the anaesthetic agent, whereas in the control groups given placebo injections, no significant changes were seen, although a tendency towards even lower maternal  $P_{CO_2}$  could be noted. These results agree well with the clinical observations made that the pain relief occurring in the former groups normalized the maternal respiratory rate in approximately 80 per cent of the patients. Secondly to the maternal  $P_{CO_2}$  and pH changes, the fetal  $P_{CO_2}$  and pH mean values were found to change in the same directions. The decrease in the fetal and the maternal pH was quantitatively equal, which agrees with earlier findings (Jacobson 1970; Jacobson & Rooth 1971; Rooth *et al.* 1973) that the maternal-fetal pH difference normally tends to remain very constant between 0.10 and 0.15 pH units during the course of labour, effected as it would seem by proper variation of the fetal  $P_{CO_2}$  level. It was evident from the obtained results that the fetal, as well as the maternal, pH decrease occurring after the paracervical block was merely due to the  $P_{CO_2}$  changes and not to a metabolic acidosis, as the  $BD_{ECF}$ , plasma lactate, and plasma pyruvate mean values showed no or only small variations.

In an attempt to evaluate the significance of the acid-base changes, the series of patients given the active anaesthetic drug was divided into two groups according to the appearance or non-appearance of transient fetal bradycardia. It was then found that the maternal and fetal  $P_{CO_2}$  and pH changes were significantly related to the bradycardia group, whereas in the non-bradycardia group, both the maternal and the fetal acid-base components showed only small and non-significant changes. An important finding was that the initial maternal  $P_{CO_2}$  mean value immediately before the block was significantly lower and the pH mean value significantly higher in the bradycardia group than in the non-bradycardia group (22  $\bar{v}$ . 27 mm Hg, and 7.51  $\bar{v}$ . 7.47), the mothers of the former group thus being more hyperventilating. Therefore the normalization of their respiratory pattern after the pain relief resulted in a quantitatively larger  $P_{CO_2}$  increase and a larger pH fall than occurred concerning the mothers in the non-bradycardia group. The same applied to the corresponding fetal  $P_{CO_2}$  and pH mean values in the two groups. It is worth noting in this context that the few patients where the paracervical block failed to give acceptable pain relief were found in the non-bradycardia group. The exclusion of these cases did not result in changed mean values of the different components determined in this group.

Different hypotheses have been advanced on the cause or causes of post-paracervical block fetal bradycardia. Usually, fetal acidosis has been considered a consequence of the bradycardia or of the effects induced on the utero-placental circulation by the anaesthetic drug (see review by Thiery & Vroman 1972). A direct toxic action of the drug on the fetal myocardium or central nervous system has also been discussed (Teramo 1971; Gennser 1972). The present investigation, however, suggests that fetal bradycardia appears as a combined effect of lidocaine and the sudden fetal pH decrease caused by the sudden maternal pH fall, which in its turn is due to the almost instant normalization of the maternal respiration rate at the pain relief. It was shown by Anderson *et al.* (1970) and by Gennser (1972) on isolated fetal heart preparations that a decrease in the pH value in the perfusion medium may augment the depressing influence of local anaesthetic drugs on the fetal heart functions, particularly as far as the active systolic pressure, the atrioventricular, and the intraventricular conduction time are concerned. It has also been shown by several investigators (see Gennser 1972) that a decrease in the pH *per se* could under experimental conditions depress the contraction frequency of the fetal heart. The assumption that the fetal pH is one of the main factors in the chain of reactions that lead to fetal bradycardia after paracervical block would help to explain the high percentage of bradycardia cases in the present series, as the series is characterized by a large number of mothers presenting forced respiration because of strong pain experience and pronounced anxiety. The causal role played by the blood concentration of the anaesthetic drug for the induction of fetal bradycardia has been the subject of much attention in other investigations (cf. Teramo 1971), but this factor would seem to be of less relevance in the present series, as the amount of lidocaine given (100 mg) is comparatively very low. Furthermore, preliminary determinations of the fetal blood concentration of lidocaine 20 minutes after the block--though not reported in the results--suggested that no significant difference was present between the bradycardia and non-bradycardia group. This matter will be the subject of a subsequent, detailed report.

The maternal and fetal acid-base changes in the bradycardia group were of transient character. At the 60-minute sampling moment after the block the acid-base balance was restored or almost restored to pretreatment values concerning the total series of paracervical block. It was found (cf. Fig. 1) that the restitution of the maternal and fetal pH levels was somewhat slower in those receiving lidocaine with epinephrine than in those receiving lidocaine alone. This might be related to the observation that the duration of the anaesthesia was longer in the former group. With this exception, no significant differences were noted between the results obtained where lidocaine was given with and without epinephrine.



The components of the determined carbohydrate and lipid metabolism usually showed only small changes during the observation period, this being true for the whole series as well as for the bradycardia group. In the bradycardia group, the fetal plasma lactate mean value was moderately increased during the first 20 minutes after the block, but this should be considered in relation to a concomitant, moderate increase in the fetal plasma pyruvate concentration resulting in an unchanged lactate/pyruvate ratio, and to a moderate increase in the plasma glucose value.

The maternal plasma glycerol concentration tended to decrease in the first 20-minute period after the paracervical anaesthesia. This might be related to a reduced release of catecholamines after the pain relief.

A prominent feature found in the  $\beta$ -hydroxybutyrate concentration status was the high mean values in the maternal blood compared with the values in the fetal blood. As raised  $\beta$ -hydroxybutyrate values are mainly seen in starvation, the results might indicate that the labour situation, particularly in very anxious patients, often involves a certain degree of depleted maternal nutrition, although the maternal  $\beta$ -hydroxybutyrate concentration in no case was high enough to give any appreciable degree of metabolic acidosis.

To summarize the results of the present investigation, the most important findings would seem to be: 1) that paracervical anaesthesia with 100 mg lidocaine given in normal labour did not induce any significant changes in maternal and fetal metabolic blood components, provided that no fetal bradycardia was induced; and 2) that a strong correlation was found to be present between pronounced maternal hyperventilation at the moment when the paracervical block was applied and development of fetal bradycardia after the block. This correlation should, in our opinion, be interpreted in view of the sudden maternal and fetal acid-base changes occurring at the instant pain relief as a result of the prompt normalization of the maternal respiration. Although such a hypothesis has not previously been suggested, similar changes in the maternal and fetal acid-base balance after paracervical block are noticeable in other published series (see i. a. Teramo 1971; Asling et al. 1970). The clinical implication of maternal hyperventilation being a common predisposing factor of fetal bradycardia is obvious concerning the possibilities then offered of reducing the incidence of this side effect of paracervical anaesthesia.

The present results did not suggest any significant changes in the fetal carbohydrate and lipid metabolism indicative of impaired fetal oxygen supply. The observed acid-base changes appeared during the first 20 minutes after the paracervical block and were mainly restored to initial conditions 60 minutes after the block. At birth, four of the 30 infants in the



paracervical block series and one of the 30 infants in the placebo series had a one-minute Apgar score between 5 and 7. At 5 minutes after birth, all the infants had an Apgar score of 8-10. Despite the high rate of fetal bradycardia encountered in this series, the bradycardia and the related fetal acid-base changes would thus seem to signify a low risk to these infants. It should be mentioned, however, that in a few individual cases in the bradycardia group the determined values of the different blood components were found to deviate from the mean values in the direction towards a moderate fetal metabolic acidosis. The present study does not allow a differentiated conclusion concerning the prognostic significance of the fetal biochemical changes seen here, but the results presently obtained encourage further investigations within this field, particularly focusing on groups of cases presenting fetal bradycardia of different severity and duration. Such an extended study is in preparation.

## SUMMARY

A series of 60 obstetrically normal parturients was subjected to a double-blind investigation of the influence of paracervical block anaesthesia in the 1st stage of labour on maternal and fetal blood components of the acid-base balance, glucose, and lipid metabolism. Four groups of 15 patients received paracervical injection with 20 ml of codified solutions containing 100 mg lidocaine, 100 mg lidocaine + epinephrine 1:400,000, saline, and saline + epinephrine 1:400,000, respectively. Maternal capillary blood and fetal scalp blood were sampled 5 minutes before, and 20 and 60 minutes after the injection. The determinations included pH,  $P_{CO_2}$ ,  $BD_{ECF}$ , plasma glucose, lactate, pyruvate,  $\beta$ -hydroxybutyrate, and glycerol.

No significant changes were found in the placebo groups. In the groups receiving the anaesthetic agents, significant and equal decrease of the maternal and the fetal pH occurred during the first 20 minutes after the block. 50 per cent of cases in the paracervical anaesthesia groups developed transient fetal bradycardia. A division of these groups into bradycardia and non-bradycardia subgroups showed that the maternal and fetal pH decrease mentioned was entirely bound to the bradycardia group. The maternal pH decrease was concluded to be primary and due to a significant rise in the maternal  $P_{CO_2}$  at the pain relief, the pre-anaesthesia maternal  $P_{CO_2}$  level in the bradycardia group being significantly lower than in the non-bradycardia group. This indicates that the mothers of the former group had a more pronounced hyperventilation. The fetal pH decrease was concluded to be principally secondary to the maternal pH fall and, perhaps except in a few cases, not indicative of fetal metabolic acidosis,

although (in combination with lidocaine) obviously an important factor in the chain of reactions inducing fetal bradycardia. No significant changes were seen regarding the components of the carbohydrate and lipid metabolism.

Pronounced maternal hyperventilation (as an expression of strong pain experience and anxiety) at the moment when paracervical block is applied would thus seem to be an important predisposing factor to fetal bradycardia. The maternal and fetal acid-base changes were mainly restored to initial conditions at 60 minutes after the anaesthesia. Despite the high percentage of fetal bradycardia in this series, only four infants of the paracervical block groups showed a slight depression one minute after birth, and all infants had a normal 5-minute Apgar score.

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CHANGES IN FETAL AND MATERNAL ACID-BASE BALANCE  
AND IN BLOOD COMPONENTS OF THE CARBOHYDRATE AND  
FAT METABOLISM IN 31 CASES OF FETAL BRADYCARDIA  
AFTER PARACERVICAL BLOCK DURING LABOUR

Stig Gårdmark, Lennart Jacobson & Gösta Rooth



## INTRODUCTION

The physiological and clinical significance of the transient fetal bradycardia that is occasionally induced by paracervical block anaesthesia during labour is still open to discussion. The uncertainty and divergency of opinions concerning the possible risks to the fetus associated with this method of obstetrical anaesthesia has, particularly in recent years, led to an increased hesitation in its use. The complexity of the problem was recently elucidated by Thiery & Vroman (1972) who, in a comprehensive review, critically evaluated the data of approximately 70,000 instances of paracervical block hitherto reported in the literature. However, despite the many reports, a rather limited number of investigations have been made into the influence of paracervical block on the fetal metabolism related to the oxygen supply.

The reported metabolic studies have been restricted to the effects on the acid-base balance in the fetus and, in some investigations, also in the mother. The results of these studies might be summarized by saying that there is still disagreement on whether or not paracervical block anaesthesia per se usually induces fetal acid-base disturbances. On the other hand, most investigators think that there is a significant correlation between post-paracervical block, fetal bradycardia, and fetal acidification in terms of decreased pH and increased base deficit values in the fetal blood (cf. Teramo & Widholm 1967; Hickl & Kirchner 1968; Jung et al. 1969; Teramo 1969 a & b, 1971; Asling et al. 1970; Thiery et al. 1970; Freeman et al. 1972). The fetal pH drop was usually found to be moderate and transient. A more pronounced decrease of pH has been noted only exceptionally (Teramo & Widholm 1967; Hickl & Kirchner 1968; Jung et al. 1969; Obolensky et al. 1969; Busch & Lübbert 1970; Vasicka et al. 1971), and there is only one case reported in which the pH decrease was persistent for a longer time (Teramo 1969 b). In the low number of fetal deaths reported in association with paracervical block, no relevant biochemical data are available.

The maternal acid-base balance was found to be uninfluenced by the paracervical block in some of the series published (Hollmén et al. 1970; Teramo 1969 a, 1971), whereas in other series, a slight influence was seen in the sense of decreased pH and increased  $P_{CO_2}$  (Jung et al. 1969; Teramo 1969 b; Asling et al. 1970; Fischer et al. 1971). Usually, the maternal acid-base changes have not been considered to substantially influence the fetal acid-base changes. Asling et al. (1970), however, noted that the maternal pH decrease was most pronounced in those cases developing fetal bradycardia.

In a previously reported double-blind study (Jacobson & Gårdmark, 1972; Gårdmark *et al.* 1974) a strong correlation was found between maternal acid-base changes and the occurrence of fetal bradycardia after paracervical block with 100 mg lidocaine. We observed that in those cases where fetal bradycardia was developed, the maternal  $P_{CO_2}$  was extremely low before the block was applied and rose very quickly after the block. We suggested that the very fast maternal pH decrease that will occur in extremely hyperventilating parturients at an instant pain relief, secondarily causing a rapid pH decrease of equal degree in the fetus, would seem to be a very common and important mechanism associated with the induction of fetal bradycardia after paracervical block. A recent study by Koepcke & Seidenschneur (1973) supports this view.

The present paper presents a detailed analysis of the fetal and maternal acid-base changes found in an extended series of fetal bradycardia cases after paracervical block with lidocaine. The study, aimed at evaluating the significance of those fetal heart reactions in terms of disturbances of the fetal oxygen supply, includes determinations of plasma lactate, pyruvate, glucose, and glycerol. No similar study seems to have appeared previously.

## MATERIAL AND METHODS

The material comprises 31 parturients, aged 30 or younger. In all cases, fetal bradycardia of varying degree occurred after paracervical block during labour. The series thus forms a part of a greater series of patients investigated for the effects of this anaesthesia method. The patients of the present series were all except one nulliparae, and the course of labour was entirely normal when the block was applied. All were given the paracervical block because they experienced the labour as very painful.

All blocks were made by the same person and with the same technique, i. e. transvaginally as a two-sites injection by means of a very short Kobak needle with an injection depth of less than 3 mm. The local anaesthetic was 0.5% lidocaine (Xylocain®) in 25 blocks and 0.5% lidocaine with epinephrine 1:400,000 in 6 blocks. Between 7 and 20 ml of the anaesthetic solution was given (= 35-100 mg lidocaine), 20 ml being the dose, used in most cases. On average, the duration of the anaesthesia was approximately 1 hour.

In five patients, delivery was terminated by means of a low vacuum extraction; the remaining cases were spontaneously delivered. Fetal scalp

blood and arterialized capillary blood from the mother's fingertip were simultaneously sampled as follows:

- 1) immediately before the block (in all cases except one)
- 2) 10 minutes after the block (in 15 blocks)
- 3) 20 minutes after the block (in 30 blocks)
- 4) 60 minutes after the block (in 28 blocks)

Tha scalp blood was anaerobically collected in 20 cm long, heparinized glass capillaries. The maternal blood was collected into short heparinized glass tubes (for the pH,  $P_{CO_2}$ , and  $SaO_2$  determinations), and in small plastic tubes adapted for the Beckman high speed micro-centrifuge (for the lactate, pyruvate, glucose, and glycerol determinations).

The fetal heart rate (FHR) was monitored in half of the cases by means of a scalp electrode and a Roche Cardiotochograph Monitor V; in the other half, FHR was registered by continuous auscultation for the first 20 minutes after the block and by intermittent auscultation during the rest of the observation period.

Based on the recorded degree of fetal bradycardia, the series was divided into two main groups: A) Moderate bradycardia, i.e.  $FHR < 120$  but  $> 80$  bpm over a period of less than 10 minutes. This group comprises 19 cases; B) Severe bradycardia, i.e. a  $FHR \leq 80$  bpm, or being  $< 120$  bpm for a period exceeding 10 minutes. This group comprises 12 cases. In three of these, the infants had an Apgar score  $\leq 7$  at birth. Within group B, a subgroup of 8 cases was denoted as very severe bradycardia and subjected to separate analysis concerning some of the determined parameters. In these 8 cases, the FHR was continuously low, between 60-100 bpm for more than 10 minutes.

The parameters determined were: pH,  $P_{CO_2}$ ,  $BD_{ECF}$ ,  $SaO_2$ , plasma lactate, pyruvate, glucose, and glycerol. In the samples drawn at 10 minutes after the block, however, only pH,  $P_{CO_2}$ , and  $BD_{ECF}$  were determined.

pH was measured with the Radiometer glass micro-electrode unit E 5021 and pH-meter PHM 27.  $P_{CO_2}$  was determined by means of the Eschweiler micro- $CO_2$ -electrode assembly.  $BD_{ECF}$ , i.e. base deficit for the extracellular fluid compartment, was calculated from the Siggaard-Andersen alignment nomogram (1963) read at the Hb 5 g/100 ml-line.  $SaO_2$  was determined by means of the photometric micro method devised by Siggaard-Andersen, Jørgensen & Naeraa (1962). For the determinations of plasma lactate, pyruvate, glucose, and glycerol, ultra-microadaptions of ordinary enzymatic methods were used. Lactate was determined spectrophotometrically; pyruvate and glycerol fluorometrically, and glucose



colorimetrically for the final stage (see also Gårdmark, Jacobson and Rooth, 1974).

As seen above, the number of samples differs between the four sampling moments settled. In the subsequent presentation of results, mean values were calculated from all data within each of the sampling moments, whereas differences and the statistical significance of differences between the sampling periods were calculated on the basis of paired samples, unless otherwise stated.

## RESULTS

pH (Table I, II, Fig. 1). In both the moderate and the severe bradycardia group, the maternal pH mean value immediately before the PCB was high, being 7.52 in both groups. During the first 20 minutes after the block, the maternal mean pH level dropped by 0.08 pH units, the decrease being equal in the two groups and statistically highly significant ( $p < 0.001$ ). In the moderate bradycardia group, the maternal pH fall occurred already during the first 10 minutes after the block, the decrease being 0.09 pH units in that period, compared with 0.06 pH units in the severe bradycardia group. From 20 to 60 minutes after the block, the maternal pH mean value increased significantly ( $p < 0.01$ ). The 60-minute value was 7.49 in both groups which in the moderate bradycardia group was significantly lower ( $p < 0.05$ ) than the initial level before the block. No statistically significant differences were present between the maternal pH mean values at the four sampling moments in the two groups.

The fetal mean pH value before the block was almost identical (7.37, 7.38) in the two groups. In both groups, the fetal pH decreased during the first 20 minutes after the block. The pH decrease was 0.04 pH units in the moderate bradycardia group ( $p < 0.01$ ), and 0.17 pH units in the severe bradycardia group ( $p < 0.001$ ). The difference between the 20-minute values in the two groups - 7.32 and 7.21, respectively - is also highly significant. The fetal pH fall in the first 10 minutes was statistically highly significant ( $p < 0.001$ ) in the moderate bradycardia group, whereas in the severe bradycardia group, the pH drop during this short period was less significant ( $p < 0.05$ ). In the subgroup of 8 very severe bradycardia cases (Table III), the 20-minute value was 7.19, although the decrease of pH was the same (0.17 pH units) as in the severe bradycardia group. Considering the 60-minute values, the fetal pH mean level was found to have risen again, in the moderate bradycardia group to the

# MODERATE BRADYCARDIA

# SEVERE AND VERY SEVERE BRADYCARDIA

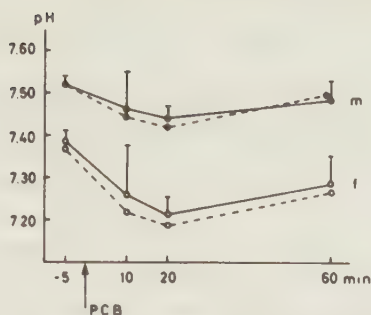
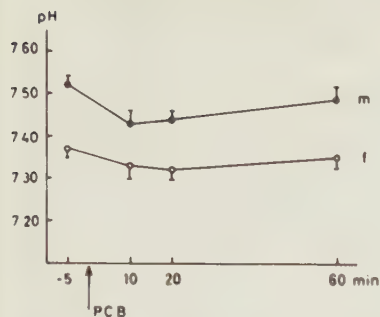


Fig 1. Fetal (f) and maternal (m) pH before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.

# MODERATE BRADYCARDIA

# SEVERE AND VERY SEVERE BRADYCARDIA

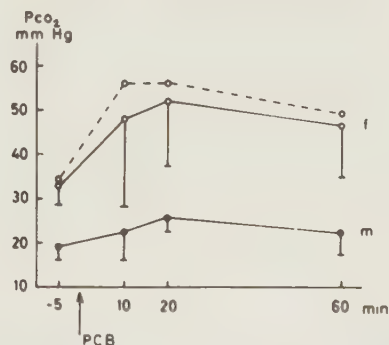
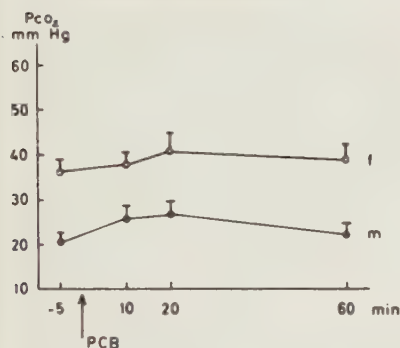


Fig 2. Fetal (f) and maternal (m)  $P_{CO_2}$  before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.

# MODERATE BRADYCARDIA

# SEVERE BRADYCARDIA

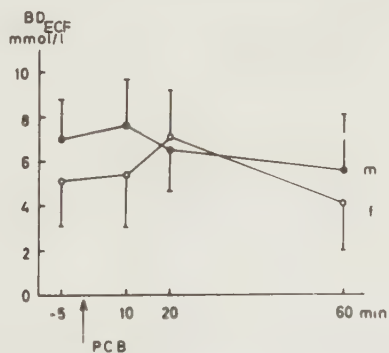
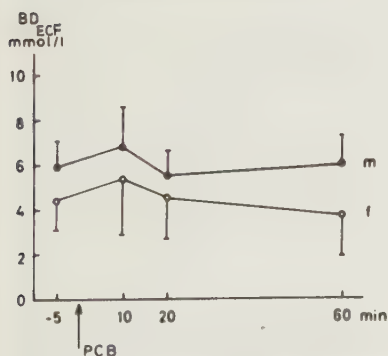


Fig 3. The fetal (f) and maternal (m) Base Deficit ( $BD_{ECF}$ ) before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.

initial value, and in the severe bradycardia group to a value below the initial level, although the difference was not statistically significant.

The mean of individual maternal-fetal pH differences (mean  $\Delta$  pH) was 0.15 pH units in the moderate bradycardia group, and 0.14 in the severe bradycardia group, immediately before the block was applied. At 20 minutes after, the mean  $\Delta$  pH was 0.12 in the moderate bradycardia group, but was increased to 0.23 pH units in the severe bradycardia group. At 60 minutes after the block, the mean  $\Delta$  pH in the two groups was 0.14 and 0.20 pH units, respectively. In the subgroup of very severe bradycardia cases, the mean  $\Delta$  pH was 0.23 pH units at 20 minutes and 0.22 pH units at 60 minutes after the anaesthesia.

Pco<sub>2</sub>. (Table I, II, Fig. 2). Immediately before the paracervical block, the maternal Pco<sub>2</sub> mean values were extremely low, around 20 mm Hg, in both groups. During the first 20 minutes after the block, the maternal Pco<sub>2</sub> mean value increased by approximately 6.5 mm Hg in both groups, the increase being statistically highly significant ( $p < 0.001$ ). The increase occurred more rapidly in the moderate bradycardia group in which the maternal Pco<sub>2</sub> was significantly higher ( $p < 0.001$ ) already 10 minutes after the block; this was not the case in the severe bradycardia group. Sixty minutes after the anaesthesia, the mean Pco<sub>2</sub> had decreased to 22-23 mm Hg in both groups, these values did not differ significantly from the initial values.

The fetal Pco<sub>2</sub> mean value increased modestly but significantly ( $p < 0.01$ ) by approximately 5 mm Hg during the first 20 minutes after the block in the moderate bradycardia group. The increase was significant ( $p < 0.05$ ) already after 10 minutes in this group. In the severe bradycardia group, a larger increase in the fetal Pco<sub>2</sub> mean value could be seen, the increase being 15 mm Hg ( $p > 0.05$ ) and 19 mm Hg ( $p < 0.05$ ) at 10 and 20 minutes, respectively, after the block. In the very severe bradycardia group (Table III), the fetal Pco<sub>2</sub> increase was even higher (22 mm Hg at 20 minutes after the anaesthesia). The fetal Pco<sub>2</sub> mean level in the moderate bradycardia group returned almost to the initial level after 60 minutes, whereas in the severe bradycardia group, the 60-minute value was 13 mm Hg higher than the pre-anaesthesia value. Statistically, this difference was not significant, nor was the difference between the 60-minute values of the two groups (8 mm Hg).

BD<sub>ECF</sub> (Table I, II, Fig. 3). No changes were found in the maternal BD<sub>ECF</sub> mean values after the paracervical block in either of the groups. The mean values lay between 5.5 and 7.6 mmol/l throughout the observation period.

The fetal  $BD_{ECF}$  mean level remained very stable throughout the observation period in the moderate bradycardia group, no significant changes being found here. As Fig. 3 shows, the fetal  $BD_{ECF}$  level in this group was constantly lower than the maternal  $BD_{ECF}$  level. In the severe bradycardia group, however, the fetal  $BD_{ECF}$  showed a moderate and statistically significant ( $p < 0.05$ ) increase 20 minutes after the block. At this sampling moment, the fetal  $BD_{ECF}$  value exceeded the maternal mean value. At 60 minutes after block, the fetal  $BD_{ECF}$  mean value in this group had fallen again to the initial level and was thus again below the maternal level. A comparison of the fetal  $BD_{ECF}$  mean values at the different sampling moments in the two series revealed no statistically significant differences.

Plasma glucose (Table I, II, Fig. 4). In the moderate bradycardia group, no significant changes were found throughout the observation period concerning the maternal and fetal plasma glucose concentration. In the severe bradycardia group, however, both fetal and maternal plasma glucose mean concentration rose significantly ( $p < 0.05$ ) in the first 20 minutes after the block, and then remained almost stable on this level. No statistically significant differences were found between the two groups in the mean values of maternal and fetal plasma glucose concentration.

Plasma lactate (Table I, II, Fig. 5). The maternal plasma lactate mean concentration did not change significantly in either of the groups during the observation period. The mean levels were found to lie between 2.4 and 4.0 mmol/l. A slightly decreasing tendency was noted in the mean values at 20 minutes after the block.

The mean fetal plasma lactate concentration was found to rise significantly during the first 20 minutes after the block in both groups. The initial values before the PCB were in both groups almost identical with the maternal ones. In the moderate bradycardia group, the fetal plasma lactate value rose from 3.3 mmol/l initially to 4.2 mmol/l at 20 minutes after the block ( $p < 0.01$ ). In the severe bradycardia group, there was a corresponding increase from 4.1 mmol/l to 8.2 mmol/l at 20 minutes after the anaesthesia, this increase being highly significant ( $p < 0.001$ ). The 20-minute mean value in the latter group differed significantly ( $p < 0.01$ ) from the 20-minute mean value in the moderate bradycardia group. At 60 minutes after the block, the fetal plasma lactate concentration was still significantly ( $p < 0.01$ ) higher in the severe bradycardia group than in the moderate bradycardia group (7.2 v. 4.2 mmol/l). The changes seen in fetal plasma lactate concentration in the very severe bradycardia group (Table III) were almost identical with those seen in the severe bradycardia group.

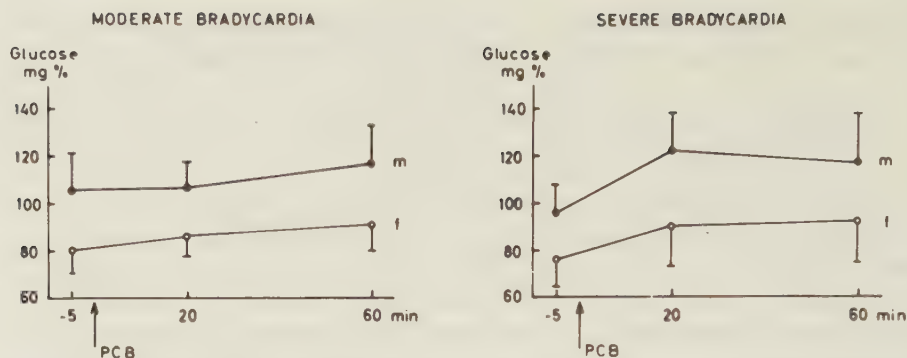


Fig 4. The fetal (f) and maternal (m) plasma glucose concentration before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.

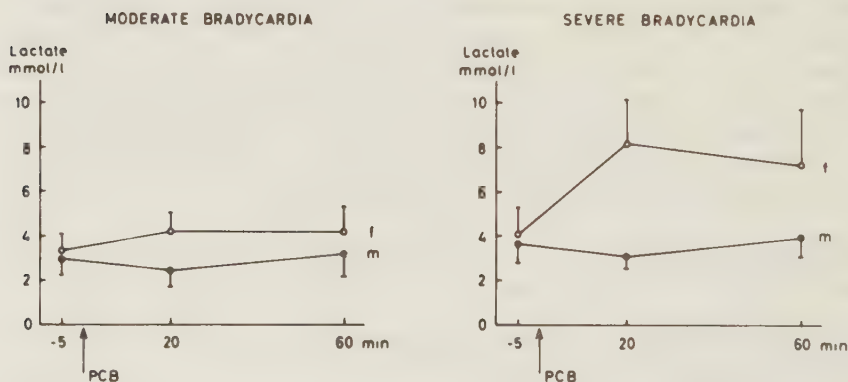


Fig 5. The fetal (f) and maternal (m) plasma lactate concentration before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.

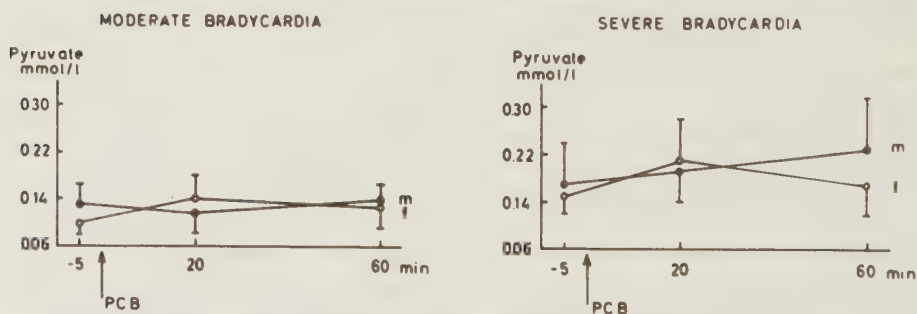


Fig 6. The fetal (f) and maternal (m) plasma pyruvate concentration before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.



Plasma pyruvate (Table I, II, Fig. 6). The maternal plasma pyruvate mean concentration was constant during the whole observation period in the moderate bradycardia group. In the severe bradycardia group, the maternal plasma pyruvate value successively increased at 20 and 60 minutes after the block, but the increase was not statistically significant. On the other hand, the 20 and 60-minute values in this group were significantly ( $p < 0.05$ ) higher than corresponding values in the moderate bradycardia group.

The fetal plasma pyruvate concentration was moderately but significantly increased during the first 20 minutes after the block, and at that sampling moment in both series exceeded the mean maternal value ( $p < 0.05$  for the increase in the moderate bradycardia group and  $p < 0.01$  in the severe bradycardia group). At 60 minutes after the block, fetal plasma pyruvate concentration was decreased in both series, resulting in mean values lower than the maternal ones.

Lactate/pyruvate ratio (L/P ratio). (Fig. 7). The maternal L/P ratio showed a slight and non-significant decrease after the PCB in both groups.

The fetal L/P ratio decreased slightly and non-significantly throughout the observation period in the moderate bradycardia group. In the severe bradycardia group, the mean value of the fetal L/P ratio increased from 32 before the block to 50 at 20 minutes after the block. The increase was not statistically significant. At 60 minutes after the block, the fetal L/P ratio decreased to 45.

Plasma glycerol (Table I, II, Fig. 8). A pronounced decrease in the maternal plasma glycerol mean concentration was found to occur during the first 20 minutes after the block in both groups. In the moderate bradycardia group, the decrease went from 0.19 mmol/l to 0.14 mmol/l ( $p < 0.01$ ), and in the severe bradycardia group from 0.26 mmol/l to 0.18 mmol/l ( $p < 0.05$ ). No significant differences were present between the 20-minute and the 60-minute mean values in either of the groups.

The mean fetal plasma glycerol concentration showed in the moderate bradycardia group a slight and non-significant increase during the whole observation period. In the severe bradycardia group, the fetal plasma glycerol value showed a more pronounced rise during the first 20 minutes after the block, the mean values increasing from 0.074 mmol/l to 0.110 mmol/l, but the increase was not statistically significant. On the other hand, the 20-minute value of the severe bradycardia group differed significantly ( $p < 0.05$ ) from the corresponding value in the moderate bradycardia group. In the very severe bradycardia group (Table III), the fetal plasma glycerol concentration increased more during the first 20 minutes after

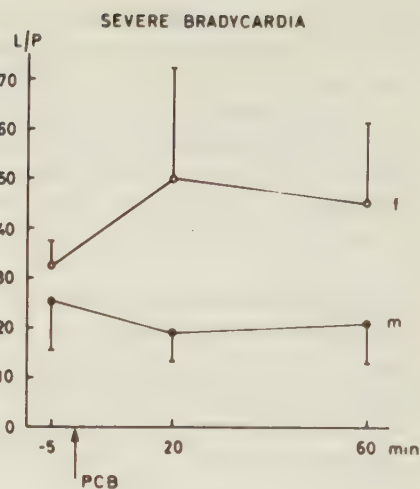
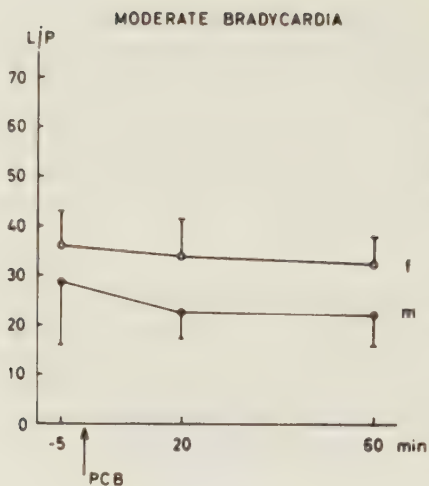


Fig 7. The fetal (f) and maternal (m) lactate/pyruvate ratio before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.

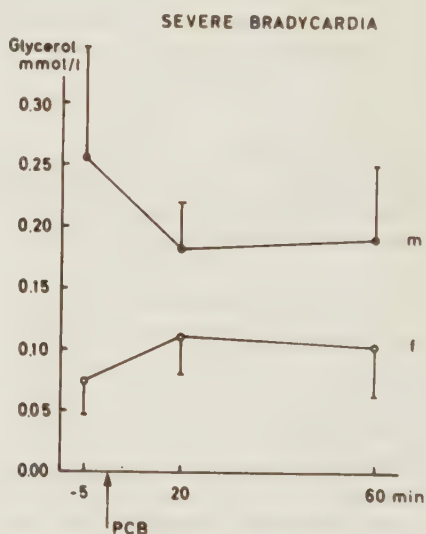
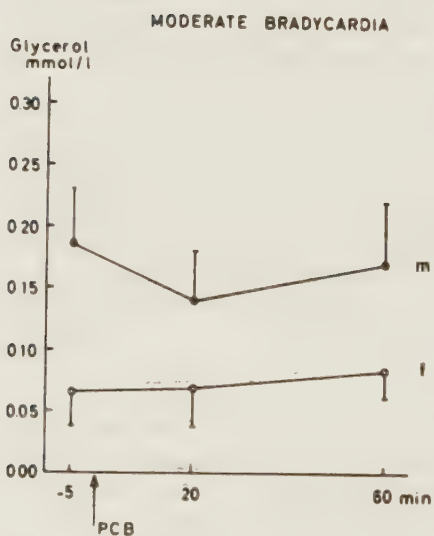


Fig 8. The fetal (f) and maternal (m) plasma glycerol concentration before and after PCB in the different groups of fetal bradycardia. Means and upper/lower 95 % confidence limits of the means.

Table I. Different maternal and fetal blood components in the group of moderate bradycardia (1) before the block, (2) 10 min after the block, (3) 20 min after the block, (4) 60 min after the block. Means and standard deviations.

|                              |           | Fetus |      |       |       | Mother |      |       |       |
|------------------------------|-----------|-------|------|-------|-------|--------|------|-------|-------|
|                              |           | 1     | 2    | 3     | 4     | 1      | 2    | 3     | 4     |
| pH                           | $\bar{x}$ | 7.37  | 7.33 | 7.32  | 7.35  | 7.52   | 7.43 | 7.44  | 7.49  |
|                              | sd        | 0.05  | 0.04 | 0.03  | 0.04  | 0.05   | 0.04 | 0.03  | 0.06  |
|                              | n         | 19    | 9    | 19    | 17    | 19     | 9    | 19    | 17    |
| Pco <sub>2</sub><br>mm Hg    | $\bar{x}$ | 35.7  | 38.4 | 41.3  | 39.0  | 20.5   | 25.6 | 26.9  | 22.2  |
|                              | sd        | 4.6   | 3.6  | 7.8   | 6.8   | 4.3    | 3.5  | 4.1   | 4.5   |
|                              | n         | 19    | 8    | 18    | 16    | 19     | 8    | 18    | 16    |
| BD <sub>ECF</sub><br>mmol/l  | $\bar{x}$ | 4.4   | 5.4  | 4.5   | 3.7   | 5.9    | 6.8  | 5.5   | 5.9   |
|                              | sd        | 2.7   | 3.0  | 3.6   | 3.3   | 2.5    | 2.1  | 2.2   | 2.3   |
|                              | n         | 19    | 8    | 18    | 16    | 19     | 8    | 18    | 16    |
| SaO <sub>2</sub><br>per cent | $\bar{x}$ | 59    |      | 57    | 56    |        |      |       |       |
|                              | sd        | 11    |      | 12    | 16    |        |      |       |       |
|                              | n         | 10    |      | 10    | 8     |        |      |       |       |
| Glucose<br>mg%               | $\bar{x}$ | 80    |      | 86    | 91    | 107    |      | 107   | 118   |
|                              | sd        | 15    |      | 14    | 18    | 28     |      | 18    | 27    |
|                              | n         | 17    |      | 17    | 15    | 15     |      | 15    | 14    |
| Lactate<br>mmol/l            | $\bar{x}$ | 3.3   |      | 4.2   | 4.2   | 3.0    |      | 2.4   | 3.2   |
|                              | sd        | 1.6   |      | 1.8   | 2.2   | 1.6    |      | 1.4   | 1.8   |
|                              | n         | 18    |      | 18    | 16    | 18     |      | 18    | 16    |
| Pyruvate<br>mmol/l           | $\bar{x}$ | 0.10  |      | 0.14  | 0.13  | 0.13   |      | 0.12  | 0.14  |
|                              | sd        | 0.04  |      | 0.09  | 0.07  | 0.07   |      | 0.07  | 0.05  |
|                              | n         | 18    |      | 18    | 16    | 18     |      | 17    | 16    |
| Glycerol<br>mmol/l           | $\bar{x}$ | 0.064 |      | 0.068 | 0.083 | 0.187  |      | 0.139 | 0.170 |
|                              | sd        | 0.038 |      | 0.044 | 0.025 | 0.063  |      | 0.058 | 0.068 |
|                              | n         | 10    |      | 10    | 9     | 10     |      | 10    | 9     |

Table II. Different maternal and fetal blood components in the group of severe bradycardia, (1) before the block, (2) 10 min after the block, (3) 20 min after the block, (4) 60 min after the block. Means and standard deviations.

|                              |           | Fetus |      |       |       | Mother |      |       |       |
|------------------------------|-----------|-------|------|-------|-------|--------|------|-------|-------|
|                              |           | 1     | 2    | 3     | 4     | 1      | 2    | 3     | 4     |
| pH                           | $\bar{x}$ | 7.38  | 7.26 | 7.21  | 7.29  | 7.52   | 7.46 | 7.44  | 7.49  |
|                              | sd        | 0.05  | 0.10 | 0.08  | 0.11  | 0.03   | 0.08 | 0.05  | 0.07  |
|                              | n         | 11    | 5    | 11    | 11    | 11     | 5    | 11    | 11    |
| Pco <sub>2</sub><br>mm Hg    | $\bar{x}$ | 33.5  | 48.1 | 52.4  | 46.6  | 19.0   | 22.6 | 25.7  | 22.7  |
|                              | sd        | 5.8   | 15.9 | 20.6  | 16.4  | 4.3    | 5.2  | 5.0   | 5.6   |
|                              | n         | 11    | 5    | 11    | 10    | 11     | 5    | 11    | 10    |
| BD <sub>ECF</sub><br>mmol/l  | $\bar{x}$ | 5.1   | 5.4  | 7.1   | 4.1   | 7.0    | 7.6  | 6.5   | 5.6   |
|                              | sd        | 3.0   | 1.9  | 3.2   | 2.9   | 2.8    | 1.7  | 2.6   | 3.5   |
|                              | n         | 11    | 5    | 11    | 10    | 11     | 5    | 11    | 10    |
| SaO <sub>2</sub><br>per cent | $\bar{x}$ | 48    |      | 42    | 348   |        |      |       |       |
|                              | sd        | 19    |      | 20    | 10    |        |      |       |       |
|                              | n         | 5     |      | 5     | 3     |        |      |       |       |
| Glucose<br>mg%               | $\bar{x}$ | 77    |      | 99    | 91    | 96     |      | 122   | 116   |
|                              | sd        | 19    |      | 26    | 22    | 21     |      | 25    | 29    |
|                              | n         | 11    |      | 11    | 10    | 11     |      | 11    | 10    |
| Lactate<br>mmol/l            | $\bar{x}$ | 4.1   |      | 8.2   | 7.2   | 3.7    |      | 3.1   | 4.0   |
|                              | sd        | 1.8   |      | 2.8   | 3.5   | 1.3    |      | 0.8   | 1.3   |
|                              | n         | 11    |      | 11    | 10    | 11     |      | 10    | 10    |
| Pyruvate<br>mmol/l           | $\bar{x}$ | 0.13  |      | 0.21  | 0.17  | 0.18   |      | 0.19  | 0.23  |
|                              | sd        | 0.05  |      | 0.11  | 0.06  | 0.10   |      | 0.07  | 0.12  |
|                              | n         | 11    |      | 11    | 10    | 11     |      | 11    | 10    |
| Glycerol<br>mmol/l           | $\bar{x}$ | 0.074 |      | 0.110 | 0.104 | 0.256  |      | 0.182 | 0.190 |
|                              | sd        | 0.027 |      | 0.035 | 0.050 | 0.104  |      | 0.047 | 0.076 |
|                              | n         | 7     |      | 7     | 9     | 8      |      | 8     | 9     |

Table III. Different maternal and fetal blood components in the group of very severe bradycardia, (1) before the block, (2) 10 min after the block, (3) 20 min after the block, (4) 60 min after the block. Means and standard deviations.

|                             |           | 1     | 2    | 3     | 4     | 1     | 2    | 3     | 4     |
|-----------------------------|-----------|-------|------|-------|-------|-------|------|-------|-------|
| pH                          | $\bar{x}$ | 7.36  | 7.22 | 7.19  | 7.27  | 7.52  | 7.45 | 7.43  | 7.50  |
|                             | sd        | 0.04  | 0.11 | 0.08  | 0.12  | 0.03  | 0.10 | 0.05  | 0.07  |
|                             | n         | 7     | 3    | 7     | 8     | 7     | 3    | 7     | 8     |
| Pco <sub>2</sub><br>mm Hg   | $\bar{x}$ | 34.9  | 56.0 | 56.5  | 48.5  | 19.9  | 22.8 | 27.2  | 23.6  |
|                             | sd        | 6.7   | 16.4 | 25.0  | 19.3  | 5.3   | 7.3  | 5.5   | 6.2   |
|                             | n         | 7     | 3    | 7     | 7     | 7     | 3    | 7     | 7     |
| BD <sub>ECF</sub><br>mmol/l | $\bar{x}$ | 5.3   | 5.0  | 6.9   | 4.1   | 6.4   | 8.0  | 6.1   | 4.6   |
|                             | sd        | 3.7   | 2.5  | 3.5   | 3.5   | 3.4   | 2.2  | 3.2   | 3.8   |
|                             | n         | 7     | 3    | 7     | 7     | 7     | 3    | 7     | 7     |
| Glucose<br>mg%              | $\bar{x}$ | 80    |      | 93    | 92    | 99    |      | 125   | 117   |
|                             | sd        | 24    |      | 26    | 27    | 26    |      | 28    | 36    |
|                             | n         | 7     |      | 7     | 7     | 7     |      | 7     | 7     |
| Lactate<br>mmol/l           | $\bar{x}$ | 4.5   |      | 8.5   | 7.7   | 4.0   |      | 3.1   | 4.2   |
|                             | sd        | 2.0   |      | 2.6   | 3.2   | 1.5   |      | 0.9   | 1.5   |
|                             | n         | 7     |      | 7     | 7     | 7     |      | 7     | 7     |
| Pyruvate<br>mmol/l          | $\bar{x}$ | 0.14  |      | 0.22  | 0.18  | 0.19  |      | 0.20  | 0.23  |
|                             | sd        | 0.05  |      | 0.12  | 0.07  | 0.12  |      | 0.08  | 0.14  |
|                             | n         | 7     |      | 7     | 7     | 7     |      | 7     | 7     |
| Glycerol<br>mmol/l          | $\bar{x}$ | 0.065 |      | 0.120 | 0.116 | 0.286 |      | 0.196 | 0.204 |
|                             | sd        | 0.027 |      | 0.035 | 0.051 | 0.103 |      | 0.042 | 0.082 |
|                             | n         | 5     |      | 5     | 7     | 6     |      | 6     | 7     |



the block than in the severe bradycardia group (from 0.065 to 0.120 mmol/l) and remained stable until the 60-minute sampling period. Because of the few paired samples, only the plasma glycerol increase from the initial sampling moment to the 60-minute sampling moment was suitable for statistical analysis. That increase was found to be highly significant ( $p < 0.001$ ).

Oxygen saturation ( $\text{SaO}_2$ ) (Table I, II). In the moderate bradycardia group, the mean  $\text{SaO}_2$  value of the fetal blood remained stable between 56 and 59 % saturation during the entire observation period. In the severe bradycardia group, the mean oxygen saturation value decreased during the first 20 minutes after the block from 48 to 42 % saturation, which is not statistically significant. From 20 to 60 minutes after the block, the fetal  $\text{SaO}_2$  value in this group increased again to the initial value. Although the oxygen saturation values throughout labour were lower in the severe bradycardia group than in the moderate bradycardia group, the differences between the groups were not statistically significant.

## COMMENTS

In the present series, comprising 31 cases of fetal bradycardia after paracervical block with small to moderate doses of lidocaine ( $\leq 100$  mg), one of the most prominent features is the very low mean value of maternal  $\text{Pco}_2$  at the moment the anaesthesia was applied. The mean value ( $20 \pm 4$  mm Hg) indicates that the mothers of this series were extremely hyperventilating before the block. After the block, i.e. at the pain relief, the maternal  $\text{Pco}_2$  level rose very rapidly, causing a sudden drop in the maternal pH and secondarily a decrease of the fetal pH. This occurred concomitantly with the development of the fetal bradycardia, and agreed with the observations made in a smaller series previously reported by us.

A division of the series into two groups on the basis of the severity and duration of the fetal bradycardia showed that the pattern of changes pertaining to the different metabolic components was different in several respects. In the group of moderate bradycardia cases, the mean values of all the components changed quantitatively much less than did the values in the group of severe bradycardia cases. From this, we concluded that moderate bradycardia in this series was neither correlated with any fetal metabolic acidosis, nor with any decrease in fetal oxygen saturation. It was noticeable that in the moderate bradycardia group, both the maternal and the fetal pH and  $\text{Pco}_2$  changes occurred more rapidly after the para-

cervical block than in the severe bradycardia group. This might be related to the fact that the maternal  $P_{CO_2}$  before the block was on average not as low in the former group as in the latter, the respiratory pattern of the mothers in the former group therefore perhaps being able to normalize somewhat faster after the instant pain relief.

The metabolic changes seen in the severe bradycardia group were thus quantitatively larger and should be commented on in more detail. The changes found in the fetal acid-base balance during the first 20 minutes after the block suggest a moderate metabolic acidosis as shown in the rise of the fetal  $BD_{ECF}$  level above the maternal level and in the increase in the fetal plasma lactate concentration and in the raised L/P ratio. The fetal oxygen saturation tended to be lower in this group than in the moderate bradycardia group, although the difference was not statistically significant.

It has been reported (Stembera & Hodr 1966) that moderate fetal hypoxia might be correlated with an increase in the plasma glucose concentration. The significant increase in the fetal plasma glucose value seen 20 minutes after the block in the severe bradycardia group is difficult to interpret in this respect, as it might also be secondary to the significant rise in the maternal plasma glucose level.

More interesting are the changes found in plasma glycerol concentration. As suggested by Šabata (1970) from umbilical cord blood studies, the fetal plasma glycerol value will rise in hypoxic situations. In the severe bradycardia group, the plasma glycerol concentration in the fetal blood at 20 minutes after the block was increased, the mean value significantly exceeding the corresponding value in the moderate bradycardia group. This tendency was even more pronounced in the subgroup of very severe bradycardia cases. The concomitant and significant fall of the maternal plasma glycerol concentration during the first 20 minutes after the block should reasonably be considered to be an effect of the pain relief, causing a decrease in the maternal catecholamine release and thus a decreased lipid mobilization. According to Šabata (1970), maternal and fetal plasma glycerol changes should be expected to occur quite independently as the transplacental interchange would seem to be very slow.

The changes seen in the maternal-fetal pH difference ( $\Delta pH$ ) agree well with the changes of the other parameters. The initial, slightly raised  $\Delta pH$  values around 0.15 pH units before the block, found in both series, should be seen in relation to the very high maternal pH at that time, caused by the hyperventilation. A constant maternal-fetal  $H^+$  ion concentration difference will for mathematical reasons give a somewhat

higher value of  $\Delta$  pH at high maternal pH-values (cf. Jacobson, Gårdmark & Rooth 1974). However, concomitantly with the maternal pH fall after the block, the  $\Delta$  pH value increased above 0.20 pH units in the severe bradycardia group, which might indicate a certain degree of fetal hypoxia. The  $\Delta$  pH increase was found to be even somewhat greater in the very severe bradycardia group.

On the whole, the metabolic changes were quantitatively more pronounced in the very severe bradycardia group than in the severe bradycardia group, thus indicating a close correlation between the degree of the fetal bradycardia and the degree of biochemical disturbances. However, it was also found that in most respects the biochemical changes induced were transient and were restored at the 60-minute sampling period after the block. Yet, in the very severe bradycardia group, the restitution tended to be delayed, as seen for instance from the  $\Delta$  pH, plasma lactate, and plasma glycerol determinations.

The primary problem related to obstetrical paracervical block anaesthesia is whether, and to what extent, the fetal bradycardia occasionally induced is a sign of a deteriorated fetal oxygen supply. In the present series, the fetal bradycardia attack was scored as pronounced, i.e. the FHR being below  $\leq 80$  bpm or remaining below 120 bpm for more than 10 minutes, in 12 of the 31 cases (39 per cent), and very pronounced or severe in eight of the 31 cases (26 per cent). In these cases of pronounced fetal bradycardia, our biochemical studies unquestionably showed a development of fetal metabolic acidosis. Although this fetal metabolic reaction was on average moderate and transient, it could well suggest a certain impairment of the fetal oxygen supply during the first 20 minutes after the anaesthesia.

In attempting to judge the risks pertaining to this method of obstetrical anaesthesia, two things must be emphasized: 1) Nine of the 12 infants in the present series, showing pronounced fetal bradycardia after the paracervical block, had a normal Apgar score (8-10) at birth, and the remaining three had a one-minute score of 5-7 and a normal 5-minute score. All 19 infants in the group of less pronounced fetal bradycardia had a normal one-minute Apgar score at birth. 2) In all cases of the present series, the mothers were extremely hyperventilating (had a low  $P_{CO_2}$  and a high pH) at the moment when the block was applied. The maternal hyperventilation was most pronounced in those cases where the more severe fetal bradycardia developed. With this taken into account at the use of paracervical block anaesthesia during labour, it would seem possible to reduce substantially not only the frequency of fetal bradycardia instances as a whole, but also the frequency of those cases tending to develop more pronounced metabolic disturbances.

## SUMMARY

In a series of 31 normal parturients in whom fetal bradycardia of varying degree and duration occurred after paracervical block with lidocaine (in a dose of  $\leq 100$  mg) during the first stage of labour, maternal and fetal acid-base status (pH,  $\Delta$  pH,  $P_{CO_2}$ ,  $BD_{ECF}$ ), plasma glucose, lactate, pyruvate, glycerol, and fetal blood oxygen saturation were determined at four sampling moments: immediately before the block, and at 10, 20, and 60 minutes after. The series was divided into two groups according to the severity of the fetal bradycardia, the groups denoted as moderate ( $n = 19$ ) and severe ( $n = 12$ ). A subgroup of very severe fetal bradycardia (8 cases) was separately analysed. It is concluded that fetal biochemical changes towards a moderate metabolic acidosis and a suspected moderate impairment of the fetal oxygen supply were correlated with fetal bradycardia scored as severe, but not with instances of moderate bradycardia. The mentioned fetal biochemical changes were quantitatively more pronounced in the group of very severe fetal bradycardia. However, the changes were principally transient and restored 60 minutes after the block, although a tendency for delayed restitution was noted in the most pronounced cases.

In previous papers, we reported on the strong correlation between extreme maternal hyperventilation before the block and the development of fetal bradycardia after the block, interpreted as an effect of the instant maternal and fetal pH fall at the sudden maternal respiratory normalization due to the pain relief. The present study further supports this observation, all the mothers having a very low  $P_{CO_2}$  before the anaesthesia. The mothers of the severe bradycardia group were found to have the lowest initial  $P_{CO_2}$  values. With this predisposing factor taken into clinical consideration, it seems possible to reduce substantially the occurrence of fetal bradycardia and fetal metabolic disturbances after paracervical anaesthesia.

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THE LIDOCAINE CONCENTRATION IN FETAL AND MATERNAL BLOOD  
AFTER OBSTETRICAL PARACERVICAL AND PUDENDAL BLOCK ANAESTHESIA, RESPECTIVELY, WITH SPECIAL REGARD TO ITS SIGNIFICANCE IN PARACERVICAL BLOCK FETAL BRADYCARDIA

Stig Gårdmark & Lennart Jacobson



The main side effect of obstetrical paracervical block anaesthesia (PCB), i.e. transient fetal bradycardia, is the subject of divergent opinions concerning its aetiology and clinical significance. Since the transplacental passage of local anaesthetics was evidenced by Bromage & Robson (1961), a great many investigations have appeared on the fetal blood concentration of these substances resulting from obstetrical conduction anaesthesia. Several studies (Gordon 1968; Shnider *et al.* 1968; Shnider & Way 1968; Asling *et al.* 1970) have suggested that the fetal blood concentration of the anaesthetic drug after PCB will be higher in cases of fetal bradycardia than in those that remain uninfluenced concerning the fetal heart rate (FHR). A correlation between low fetal blood pH values, associated with bradycardia, and high fetal blood concentrations of the anaesthetic agent has been reported by *i.a.* Asling *et al.* (1970) and Teramo & Rajamäki (1971). In some investigations, the fetal blood concentration of the local anaesthetic has been found to exceed the corresponding maternal level, particularly in cases of fetal bradycardia (Shnider *et al.* 1968; Asling *et al.* 1970; Hyman *et al.* 1971), whereas other authors have claimed that the opposite is the rule (cf. Gordon 1968; Hollmén *et al.* 1969; Taylor *et al.* 1970; Teramo & Rajamäki 1971; Thiery & Vroman 1972). However, it should be noted that the published investigations differ in many respects: for instance, the anaesthetic drug used, the total dose administered, and the assay methods applied for determination of the blood concentrations, rendering comparative interpretations of the results more difficult. Other factors and mechanisms have also been suggested as possible causes of fetal bradycardia after PCB, such as constriction of the placental vessels, mechanical compression of the uterine vessels, changes in the myometrial activity, and increased pressure on the fetal skull induced by the anaesthesia procedure (see review by Thiery & Vroman 1972).

Several facts argue against the idea that induction of the paracervical block fetal bradycardia is directly related to the fetal blood concentration of the drug. For instance, the correlation between the frequency of fetal bradycardia and the total dose of administered anaesthetic is seen to vary rather widely between different series. Also, the frequency of bradycardia would not seem to be higher in series of continuous paracervical block anaesthesia. It is further noticeable that fetal bradycardia is seldom encountered in obstetrical pudendal blocks, despite the doses of local anaesthetics administered at this kind of block anaesthesia being of the same magnitude as those used at PCB.

In series previously reported on by us (Gårdmark *et al.* 1974 a, b) a high rate of fetal bradycardia (around 50 %) was noted after PCB despite the use of low or very low doses of lidocaine ( $\leq 100$  mg); the drug, moreover, being injected at a depth of only 2–3 mm below the mucosal surface. However, we found that fetal bradycardia in those series occurred mainly in



patients excessively hyperventilating at the time PCB was applied. The maternal acid-base balance in these cases was characterized by a very low  $P_{CO_2}$  and a high pH level. As a result of the immediate pain relief, a prompt rise of the maternal  $P_{CO_2}$  and a fall of the maternal pH occurred, the latter secondarily causing a similar decrease in the fetal pH (i.e. the  $\Delta pH$  value remained constant). In mothers not extremely hyperventilating, fetal bradycardia did not develop, and the acid-base changes were slight (cf. Fig. 1). It was suggested that the fetal pH fall induced by the fast normalization of the respiratory pattern in the highly hyperventilating mothers after the PCB might be an important part of the mechanisms, initiating fetal bradycardia, and active independently of the blood concentration of the drug.

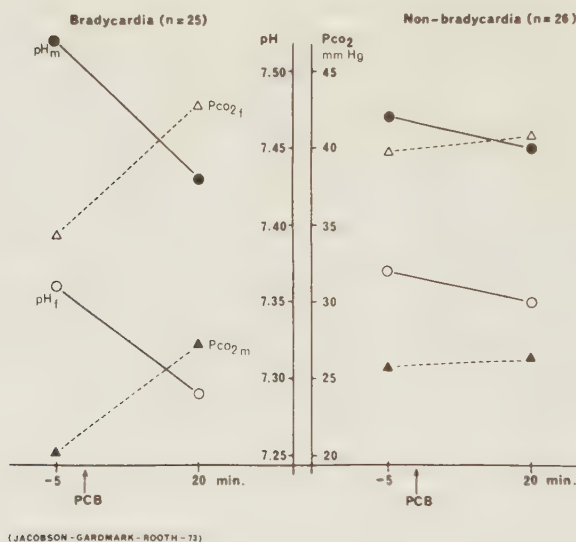


Fig 1. Fetal and maternal blood pH and  $P_{CO_2}$  before and after paracervical block anaesthesia in a group of cases developing fetal bradycardia and in a group not developing fetal heart rate changes (from Jacobson *et al.* 1973).

The present investigation complements the previous ones, being aimed at determining, in a series of PCB cases, the fetal and maternal blood concentration of lidocaine in bradycardia and non-bradycardia cases, respectively, and also at studying, in an identical way, the lidocaine blood concentrations appearing after pudendal block anaesthesia, using the same dose of anaesthetic.

## MATERIAL AND METHODS

The study includes two series.

### A) Series of paracervical block anaesthesia.

The series comprises 23 parturients, aged 18-32 (mean 24) years, and partly identical with the previously reported series of PCB, referred to above. All patients were nulliparae, and the labour was obstetrically uncomplicated at the time the anaesthesia was given. The PCB was applied in the first stage of labour at a cervical dilatation of 3-5 cm, in all cases by the same person and with the same technique, using an extremely short Kobak needle to ensure an injection depth of 2-3 mm. In all except three patients, a total dose of 20 ml 0.5% lidocaine (Xylocain®) solution without epinephrine was administered: one receiving 18 ml of the same solution; the other two, 15 ml.

Fetal monitoring by means of scalp electrode and a Roche Cardiotocograph V, in combination with continuous intrauterine pressure recording; was constantly performed. In ten of the cases fetal bradycardia followed the PCB. Bradycardia in this series is defined as a base-line bradycardia (< 120 bpm) with a duration of 3-10 minutes. The fetal bradycardia appeared on average within 5 minutes after the block anaesthesia. The infants were all subsequently delivered in a vigorous state (one-minute Apgar score 8-10). The birth weights ranged between 2,630 and 4,300 g (mean 3,340 g).

### B) Series of pudendal block anaesthesia.

The series comprises 18 parturients, all nulliparae and presenting an uncomplicated course of labour at the time the anaesthesia was given. The age of the mothers ranged between 18 and 32 (mean 25) years. The pudendal block was applied by transvaginal technique at the moment the fetal head reached the pelvic floor. In all cases, 20 ml 0.5% lidocaine solution without epinephrine was administered. In no case did fetal bradycardia occur. All infants were vigorously born (one-minute Apgar score 8-10). The birth weights ranged between 3,020 and 4,340 g (mean 3,485 g).

In all the cases, fetal scalp blood was sampled at 10 and 20 minutes after the lidocaine injection. In seven in the PCB series and in 13 in the pudendal block series, samples were drawn from an antecubital vein (without application of stasis) of the mothers simultaneously with the fetal blood samplings. In addition, umbilical arterial and venous blood was drawn

from the clamped cord at birth in five cases in the pudendal block series, delivered within 10 minutes after the second fetal scalp blood sampling moment.

Each one of the fetal scalp blood samples was adjusted to amount 100  $\mu$ l which was immediately added to 3.0 ml saline solution and stored in a deep freeze. The maternal and umbilical cord blood samples, amounting to between 5 and 10 ml, were collected into heparinized glass tubes and transferred to a deep freeze until analyzed.

By courtesy of Astra Pharmaceuticals Ltd., Södertälje, Sweden, the samples were analysed for their lidocaine concentration at the Astra Research and Development Laboratories for Analytic Chemistry. The determinations were made with a micro-adapted gas chromatographic technique (Astra 1973). The accuracy of the method is high ( $\pm 0.1 \mu\text{g/ml}$ ) for concentration values  $\geq 0.2 \mu\text{g/ml}$ . In the subsequent analysis of results, all individual values  $< 0.2 \mu\text{g/ml}$  were set equal to  $0.1 \mu\text{g/ml}$ , implying a slight approximation of no practical importance. According to the assay method, the present values express the concentration of lidocaine base, these values being 15% lower than those obtained at gas chromatographic determination of lidocaine hydrochloride.

## RESULTS

A) Series of paracervical block anaesthesia (Table I, Fig. 2).

As the table and the figure show, the mean values of lidocaine concentration in fetal blood ranged between 0.3 and 0.5  $\mu\text{g/ml}$  blood. No statistically significant differences were present between the mean values at the 10 minute and the 20 minute sampling moment, nor between the mean lidocaine concentration in the bradycardia and in the non-bradycardia group. The total range of fetal values was  $< 0.2 - 1.4 \mu\text{g/ml}$ .

The maternal determinations gave the 10 minute values 0.3, 0.3, and 0.7  $\mu\text{g/ml}$ , and the 20 minute values 0.4, 0.6, and 0.7  $\mu\text{g/ml}$  in the bradycardia group. In the non-bradycardia group, the corresponding maternal concentration values found were 0.4, 0.5, 0.5, and 0.7  $\mu\text{g/ml}$ , and 0.5, 0.6, 0.7, and 0.8  $\mu\text{g/ml}$ . In all cases in the series, the maternal concentration values exceeded the corresponding fetal values.

B) Series of pudendal block anaesthesia (Table I, Fig. 2).

The mean lidocaine concentration of fetal scalp blood was 0.2  $\mu\text{g/ml}$  at both sampling moments. The range of individual values was between  $< 0.2$  and 0.8  $\mu\text{g/ml}$ . The mean concentration in maternal blood was found to be 0.4 and 0.6  $\mu\text{g/ml}$  at 10 and 20 minutes after the block, respectively. The difference of means was statistically significant ( $p < 0.01$ ). In all individual cases, the maternal blood concentration exceeded the corresponding fetal concentration.

In five cases of umbilical cord blood determinations performed within 10 minutes after the second fetal scalp blood sampling moment, the mean values were found to be 0.1 and 2  $\mu\text{g/ml}$  for arterial and venous blood, respectively.

Table I. Mean concentration values of lidocaine (in  $\mu\text{g/ml}$  blood) found in the paracervical block and pudendal block series.

|                   |           | Paracervical block |     |                  |     | Pudendal block |     |          |
|-------------------|-----------|--------------------|-----|------------------|-----|----------------|-----|----------|
|                   |           | bradycardia        |     | non-brady-cardia |     |                |     |          |
|                   |           | 10'                | 20' | 10'              | 20' | 10'            | 20' | at birth |
| Fetal scalp blood | $\bar{x}$ | 0.5                | 0.4 | 0.4              | 0.3 | 0.2            | 0.2 |          |
|                   | sd        | 0.4                | 0.2 | 0.3              | 0.1 | 0.2            | 0.1 |          |
|                   | n         | 10                 | 10  | 13               | 13  | 18             | 18  |          |
| Maternal blood    | $\bar{x}$ | 0.4                | 0.6 | 0.5              | 0.7 | 0.4            | 0.6 |          |
|                   | sd        | 0.2                | 0.2 | 0.1              | 0.1 | 0.2            | 0.2 |          |
|                   | n         | 3                  | 3   | 4                | 4   | 13             | 13  |          |
| Umbilical artery  | $\bar{x}$ |                    |     |                  |     |                |     | 0.1      |
|                   | sd        |                    |     |                  |     |                |     | 0.1      |
|                   | n         |                    |     |                  |     |                |     | 5        |
| " vein            | $\bar{x}$ |                    |     |                  |     |                |     | 0.2      |
|                   | sd        |                    |     |                  |     |                |     | 0.1      |
|                   | n         |                    |     |                  |     |                |     | 5        |

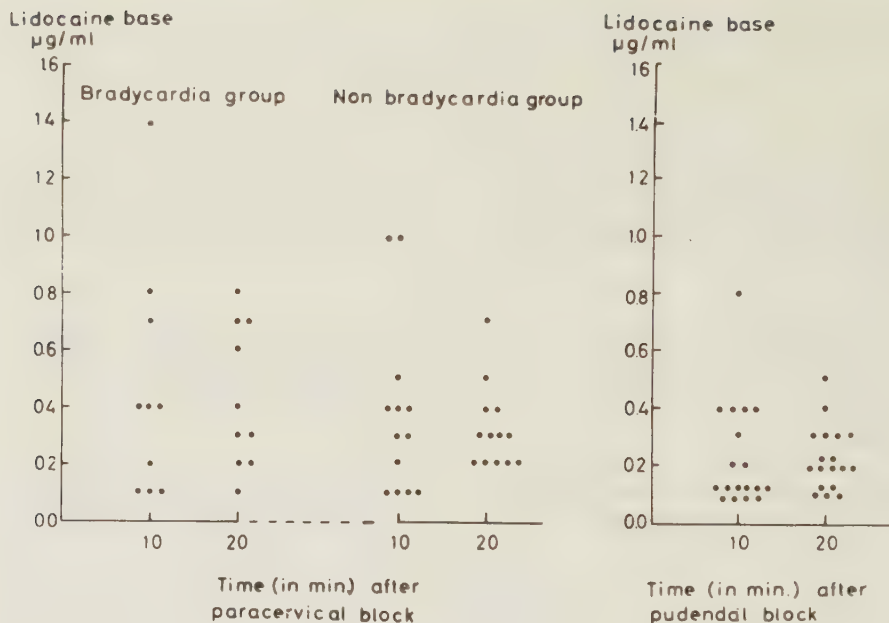


Fig 2. Distribution of lidocaine concentration values in fetal scalp blood at 10 and 20 minutes after the anaesthesia in the PCB series and in the pudendal block series.

## COMMENTS

The mean values of the lidocaine concentration in fetal and maternal blood after PCB found in the present series are distinctly lower than those reported by other investigators using gas chromatographic determination techniques, and very much lower than those obtained in studies based on complexometric and colorimetric measuring methods (see review by Thierry & Vroman 1972). Also when considering the upper range of the individual values recorded in our series, this statement holds true. Thus, for instance Shnider *et al.* (1968) and Asling *et al.* (1970), using 200 mg



mepivacaine for PCB, found fetal scalp blood mean values between 3-10 times higher and maternal blood mean values between 3-5 times higher than the present ones. Similar results were obtained in their umbilical cord blood studies. In a series of 23 cases of paracervical and pudendal blocks, Shnider & Way (1968) found that lidocaine concentrations below 2.5  $\mu\text{g/ml}$  in umbilical venous blood were not correlated with depression of the newborn at birth, the levels in moderately depressed infants consistently exceeding 3.0  $\mu\text{g/ml}$ . On the other hand, the frequency of fetal bradycardia encountered in our series of PCB is higher than that found in most other published series.

The low lidocaine concentration levels in both fetal and maternal blood in the present series might, at least in part, be attributed to the comparatively low total dose of administered lidocaine ( $\leq 100$  mg), and to the injection technique used (i.e. extremely low injection depth). The possible influence of the latter factor is suggested by the present findings that the mean concentration of lidocaine in maternal blood showed a tendency to increase during the 20 minute observation period after the block, contrary to the results obtained by Asling *et al.* (1970) which showed a concentration peak at 5 minutes and a decreasing concentration after 10 minutes, thus indicating a more rapid absorption of the drug from the injection site into the maternal circulation in their series.

In all cases of the present study, the maternal blood concentration of lidocaine exceeded the corresponding fetal blood concentration. In this respect, the results agree with those reported by *i.a.* Gordon (1968), Teramo & Rajamäki (1971), and Thiery *et al.* (1972), but disagree with those given by Shnider *et al.* (1968) and Asling *et al.* (1970) who found higher fetal than maternal blood levels in bradycardia cases and suggested in those instances the occurrence of a direct transport of the anaesthetic drug from the paracervical space to the fetus.

It is highly interesting to note that in this investigation no differences existed between the bradycardia and non-bradycardia group concerning the fetal and maternal blood concentrations of lidocaine, and also that the lidocaine mean values recorded after pudendal block anaesthesia were equal to or only slightly lower than those found after PCB. Furthermore, it is noticeable that the mean fetal blood levels of lidocaine recorded in the bradycardia cases are lower than those reported for non-bradycardia cases in other investigations.

The present results, of course, leave open the question whether a high dose and high fetal blood concentrations of a local anaesthetic might occasionally be the primary aetiological factor in paracervical block fetal bradycardia. However, they distinctly show that the appearance of

fetal bradycardia after PCB might equally well be correlated with low doses and low blood levels of the local anaesthetic agent, thus strongly suggesting that aetiological mechanisms not related to the height of the blood concentration level should be considered. The results in this respect afford additional support to the suggestion, advanced in previous studies (Gårdmark et al. 1974 a, b) and summarized initially in this paper, that paracervical block fetal bradycardia might ensue on the combined influence of the anaesthetic drug, irrespective of its concentration, and the rapid fall of the maternal and, thus of the blood pH. Such a situation, we found, is particularly apt arise after paracervical block applied in the first stage of labour in strongly hyperventilating mothers, who are in a state of respiratory alkalosis. At the pain relief, the maternal respiration will normalize almost instantly, resulting in a raised maternal blood  $P_{CO_2}$  and therefore in a fall of the maternal pH, which secondarily induces a corresponding fall of the fetal blood pH. In the second stage of labour, i. e. when pudendal blocks are applied, the presence of such prerequisites concerning maternal respiration and acid-base conditions are likely to be most unusual.

The further pharmacological interpretation of the aetiological mechanism thus suggested is purely hypothetical. There is certain evidence that absorption, anaesthetic action, and transplacental transportation of local anaesthetic substances could be influenced by changes in the environmental pH (see reviews by i. a. Löfström 1970; Teramo 1971). Furthermore, perfusion studies on the isolated fetal heart (Andersson et al. 1970; Gennser 1972) have shown that a decrease in the pH augments the depressing influence of local anaesthetics on the contraction rate and on the atrio-ventricular and intraventricular conduction time. A decrease in pH per se might similarly influence the fetal heart contraction rate (Gennser 1972). It can also be added that the uptake of local anaesthetic substances in the central nervous tissues is enhanced by acidosis (Wagman et al. 1967, and others).

A proper understanding of the pharmacological significance of fetal bradycardia after obstetrical paracervical block anaesthesia is clinically highly desirable. The results of the present study indicate, as did those of our previous investigations referred to above, that aetiological factors and mechanisms other than a blood concentration related action of the anaesthetic agents must be considered, and should be subjected to further detailed studies.

## SUMMARY

In a series of 23 obstetrically normal parturients, given paracervical block anaesthesia (PCB) with 75-100 mg lidocaine (Xylocain®) in the first stage of labour, the concentration of lidocaine in fetal and maternal blood was gas chromatographically determined. In 10 of them, fetal bradycardia during 3-10 minutes followed the PCB.

Another 18 obstetrically normal parturients given pudendal block anaesthesia in the second stage of labour with 100 mg lidocaine, were subjected to identical investigation. In five of them, lidocaine was also determined in umbilical cord blood at birth.

The mean values of lidocaine concentration in fetal and maternal blood were throughout the study very low, ranging from 0.2 to 0.7  $\mu\text{g/ml}$  blood. The range of individual values lay between  $< 0.2$  and 1.4  $\mu\text{g/ml}$ . The present values are very low compared with those reported in other investigations. The maternal lidocaine concentration always exceeded the fetal.

No significant differences of lidocaine fetal and maternal blood concentration were encountered between the bradycardia and non-bradycardia group in the PCB series. The concentration levels found in the pudendal series were equal to or slightly lower than those of the PCB series.

The results show that fetal bradycardia after PCB can well appear at low blood concentration levels of the local anaesthetic agent, thus strongly suggesting that aetiological mechanisms other than a blood concentration related toxic action of the drug on the fetal heart must be considered. Based on the present results and those of previous studies, an alternative aetiological possibility is proposed.

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INFLUENCE ON FETAL CARBOHYDRATE AND FAT METABOLISM AND  
ON ACID-BASE BALANCE BY GLUCOSE ADMINISTRATION TO THE  
MOTHER DURING LABOUR

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Key-Words: Glucose, Insulin, Lactate, Pyruvate,  $\beta$ -hydroxybutyrate,  
Glycerol, Acid-base-status, Sodium





## INTRODUCTION

Glucose administration to women in labour is used in many places in order to augment the fetal chances of survival where there is asphyxia during birth (Romney and Gabel, 1966; Paterson, Phillips and Wood, 1967; Příbylová and Znamenacek, 1970; Hüter, 1972; Šabata *et al.*, 1973). The metabolic consequences for the human fetus of such treatment are not fully known, having been studied mainly by single-point determinations of biochemical parameters in fetal blood (Paterson, Phillips and Wood, 1967; Anderson, Cordero and Hon, 1970). The opinion has recently been expressed that glucose load to parturients may adversely increase the acidosis in the oxygen-deprived fetus owing to a rise of plasma lactate (Shelley, 1973). Furthermore, the role of glucose as the predominant source of energy for fetal metabolism (Šabata, Wolf and Lausmann, 1968; Alexander *et al.*, 1969) has recently been challenged (Setchell *et al.*, 1972; Battaglia and Meschia, 1973) but the alternatives of metabolic fuel are not yet completely defined. The metabolic effects of glucose administration prenatally thus are of great physiological and clinical importance. By applying ultra-micro analytical methods on fetal scalp blood samples, it is possible to follow several simultaneous metabolic events during labour. The present investigation was performed with such technique on normal parturients in order to analyse whether glucose load influenced the fetal acid-base balance by affecting the carbohydrate and fat metabolism and to elucidate the maternal-fetal interrelationship of the metabolic responses.

## MATERIAL AND METHODS

### MATERIAL

The material comprises 13 healthy women, aged 18-31 (mean 23.7), with uncomplicated term pregnancies and normal spontaneous labour. All except one were primiparae, the birth weights of their infants ranging from 2,980 to 4,850 (mean 3,680) g. The normality of the group of patients was shown by the uneventful history of the present pregnancy, the clinical course of the delivery before and during the study, and the absence of any signs of fetal asphyxia. The newborns subsequently appeared mature with appropriate birth weights and an Apgar score of 8-10. The nature and purpose of the investigation was explained to the patients; all gave their consent.

15 primiparae with normal labour before and during the study served as controls. These patients, for other purposes, were subjected to blood sampling and determination of the same parameters as in the present investigation. In this series, fetal and maternal blood were obtained on two occasions at 60 minutes interval. The blood sampling started somewhat later in the first stage (at a cervical dilatation of 3-5 cm) and the parturients had a more painful labour than those in the series receiving glucose. Details of the control cases are reported elsewhere (Gårdmark, Jacobson and Rooth, 1974 a). The results of the analyses in the control series are expressed as means and are only reported in Figures 1-9 to demonstrate the numerical levels and changes normally occurring during the period of labour studied.

## CLINICAL PROCEDURE

The study began in the first stage of labour as soon as the position of the fetal head and the cervical dilatation permitted fetal scalp blood sampling. None of the patients experienced severe labour pains during the studied period. Two patients received 50,75 mg pethidine: one just before the beginning of the glucose administration and the other just after the end. No other analgetic drug was given during the study. In accordance with the prevailing dietary scheme of the labour ward, the patients were allowed an unrestricted liquid diet consisting of sugarsweetened juice and soup, before and during the study. The caloric intake was not measured, but was generally fairly low. The patients remained in the recumbent position during the study.

The glucose infusion was intended to give a stable elevated maternal plasma glucose concentration for one hour. To achieve a rapid plasma glucose rise, 100 cc 25 % or 120 ml 20 % glucose solution was infused into an antecubital vein as rapidly as possible. 20 % glucose solution was then continuously infused intravenously by means of an Ivac 501 infusion pump. The maternal plasma glucose concentration was monitored by frequent blood-sugar determinations with Dextrostix® test tape and Ames Reflectance Meter®, and the level was kept as constant as possible at 180-240 mg % by adjustment of the infusion speed. The maternal blood glucose level was also measured by a standard laboratory glucose oxidase method (see Analytical Methods) Thirty minutes after reaching a steady state and at the end of the infusion, the mean values were  $237 \pm 32$  mg % and  $239 \pm 31$  mg %, respectively. The total infusion time ranged from 60 to 120 (mean 88) min and the total amount of glucose given from 54 to 120 (mean 80) g.

## SAMPLE COLLECTION

Fetal and maternal capillary blood were sampled simultaneously on three occasions in each of 13 patients, i. e. (1) before beginning, (2) at the end of, and (3) thirty minutes after the end of the glucose administration. Maternal capillary blood samples were also taken for glucose determination thirty minutes after reaching steady state of maternal plasma glucose concentration. Maternal venous blood for insulin measurements was obtained from 8 women before and at 3, 5, 7, 10, 15, 30, 45, and 60 min after beginning the infusion, and 15 and 30 min after the end.

The fetal scalp blood was collected anaerobically in heparinized glass capillaries approximately 20 cm in length and connected in their outer end to a polyethylene catheter. Approximately 0.8 ml fetal capillary blood was obtained at each sampling.

For insulin determination in the mother, blood was aspirated from an antecubital vein contralaterally to the infusion arm through an indwelling catheter, and collected in EDTA-containing test tubes. For all other purposes, arterialized maternal capillary blood was sampled from a finger-tip and into short heparinized glass capillary tubes (for pH,  $P_{CO_2}$  and haemoglobin measurements) and in small plastic tubes for a Beckman high speed micro centrifuge (for plasma glucose, lactate, pyruvate,  $\beta$ -hydroxybutyrate, glycerol, and sodium determinations). The acid-base parameters were determined within a few minutes. For the other biochemical analyses, the samples were kept cool before centrifuging within 10 min, and plasma was separated and stored in a deep-freeze for a maximum of one month before further processing.

## ANALYTICAL METHODS

pH was measured by means of the Radiometer glass micro-electrode unit 5021 and pH meter PHM 27.

$P_{CO_2}$  was determined with the Eshweiler micro- $CO_2$ -electrode assembly.

Base deficit was calculated for the entire extracellular fluid compartment ( $BD_{ECF}$ ) from the Siggaard-Andersen alignment nomogram, (1963).

Table I.

|                                                             | Time after start of intravenous glucose infusion, min |              |              |              |
|-------------------------------------------------------------|-------------------------------------------------------|--------------|--------------|--------------|
|                                                             | 0                                                     | 5            | 7            | 10           |
| Plasma insulin, $\mu\text{U}/\text{ml}$                     | $45 \pm 22$                                           | $118 \pm 34$ | $110 \pm 34$ | $120 \pm 29$ |
| <hr/>                                                       |                                                       |              |              |              |
| Early Insulin Response $\mu\text{U}/\text{ml}$ $138 \pm 43$ |                                                       |              |              |              |

The Early Insulin Response (ER) to intravenous glucose load in eight women during labour, quantified according to the formula

$$\text{ER} = I_t + K \cdot \text{area}_t$$

where  $I$  is the net plasma insulin concentration, and area refers to the area under the insulin curve for 0 -  $t$  min (Thorell, Nosslin and Sterky, 1973). Sampling times were 0, 5, 7, and 10 min. Elimination constant ( $K$ ) of  $0.1 \text{ min}^{-1}$  was chosen. Mean  $\pm$  95% confidence limits of the means.



Haemoglobin (Hb) concentration was determined with a Vitatron Photometer.

Glucose was determined by the glucose oxidase method described by Marks (1959).

Lactate was determined with an ultramicro-adaptation of the slightly modified Boehringer enzymatic method (Boehringer Bulletin T C-B 972) (Rooth 1967).

$\beta$ -hydroxybutyrate ( $\beta$ -HB) was determined by the  $\beta$ -HB dehydrogenase method of Williamson *et al.* (1962) modified according to Persson (1970).

Pyruvate was determined fluorimetrically by an ultramicro-adaptation of the Boehringer enzymatic method using for the final stage a spectro-fluorometer (Boehringer Bulletin T C-B 972) (Rooth, 1967).

Glycerol was determined by an enzymatic fluorometric micro-method described by Laurell and Tibblin (1966).

Sodium was determined according to the method of Kaplan and del Carmen (1956).

Insulin was determined by radio-immunoassay with ethanol precipitation of antibodies (Heding, 1966). The insulin response to intravenous glucose load during the first 10 min (Early Insulin Response) was quantified according to Thorell, Nosslin and Sterky (1973) by the equation

$$\text{response} = I_t + k \cdot \text{area}_t \text{ (cf Table I)}$$

All results of all assays are expressed as mean values and the 95 % confidence limits of the means. The probabilities given are derived from statistical analyses of paired samples.

## RESULTS

Glucose (Fig. 1) The glucose infusion increased the maternal plasma glucose concentration from 97 mg% before to 239 mg% at the end of the glucose administration. Half an hour after the glucose infusion ended, the level was still elevated at 137 mg% ( $p < 0.01$ ).

The fetal plasma glucose concentration increased from 69 mg% to 172 mg% ( $p < 0.001$ ) during the glucose infusion. Thirty minutes after the end, the fetal glucose had decreased to 109 mg%, but was still higher than before the glucose administration ( $p < 0.01$ ).

Before the infusion, the maternal-fetal difference of plasma glucose concentration was 38 mg%. At the end of infusion, it had increased to 67 mg% ( $p < 0.001$ ). 30 min later, it was reduced to 30 mg%. The correlation between the maternal and fetal glucose levels was strong at all sampling moments;  $r = 0.76$  before, 0.90 at the end of, and 0.93 thirty minutes after the infusion.

Sodium. The maternal value of the plasma sodium concentration at the beginning of the study was  $136.4 \pm 3.1$  mmol/l, and the corresponding fetal value was  $134.4 \pm 7.1$  mmol/l. No significant changes in the maternal and fetal sodium concentration occurred during and after the glucose infusion.

Haemoglobin. The maternal haemoglobin concentration was 14.1-14.0 g/100 ml during the study; the fetal was 18 g/100 ml before, 17.9 g/100 ml at the end of, and 17.6 g/100 ml 30 min after the glucose administration ended.

Lactate (Fig. 2). The maternal plasma lactate concentration was 2.0 mmol/l before and 3.2 mmol/l at the end of the glucose infusion ( $p < 0.001$ ). Thirty minutes later the maternal lactate concentration remained elevated (3.3 mmol/l).

The initial fetal plasma lactate concentration was higher than the corresponding maternal value and remained so at all sampling moments. The fetal lactate increased from 2.7 mmol/l to 3.8 mmol/l during the glucose infusion and was still elevated 30 min after the administration ended (4.2 mmol/l).

The correlation coefficient between the fetal and maternal plasma lactate concentration was 0.13 before, 0.20 at the end of, and 0.66 thirty minutes after the glucose infusion.

Pyruvate (Fig. 3). A rise of the maternal plasma pyruvate concentration from 0.13 mmol/l to 0.25 mmol/l ( $p < 0.01$ ) occurred during the glucose infusion. Thirty minutes after the end of the administration, the maternal pyruvate was 0.22 mmol/l; this decrease was not statistically significant.

The initial fetal pyruvate concentration was 0.10 mmol/l. This level rose during the glucose administration to 0.15 mmol/l ( $p < 0.001$ ). Thirty min-

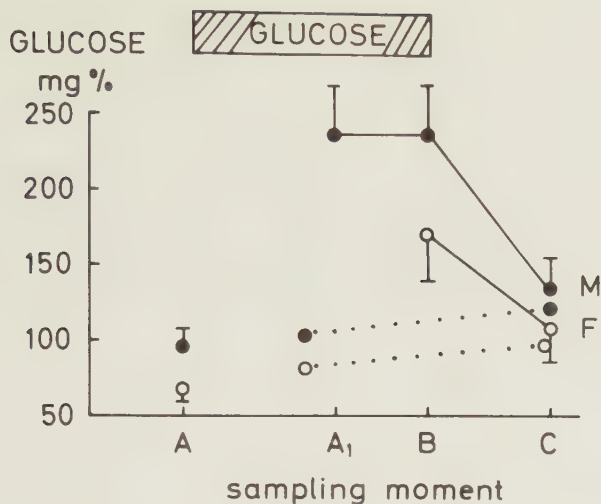


Fig 1. Glucose concentrations in maternal (●) and fetal (○) plasma before (A), during (A<sub>1</sub>), at the end of (B), and 30 min after (C), intravenous glucose infusion to the mother. Mean values and upper/lower 95 % confidence limits of the means. Symbols connected by the dotted lines represent mean values in an untreated control series at two instances with a 60 min interval during the first stage of labour (see Material).

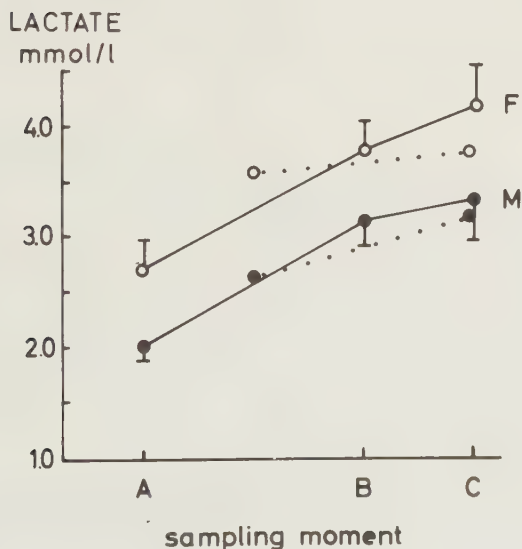


Fig 2. Maternal and fetal plasma lactate concentrations in relation to glucose infusion to the mother. Symbols as in fig. 1.

PYRUVATE  
mmol/l

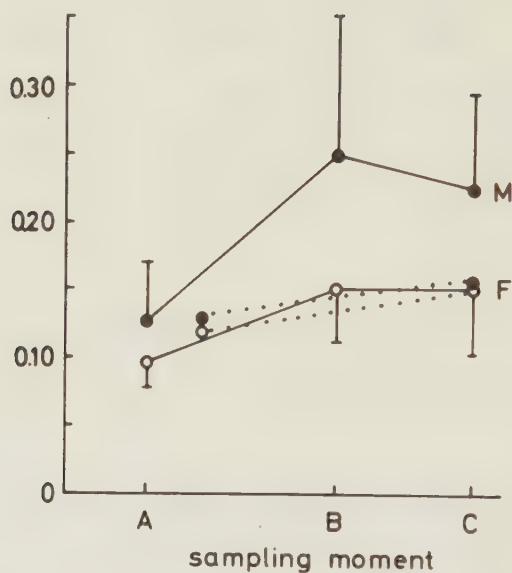


Fig 3. Maternal and fetal plasma pyruvate concentrations in relation to glucose infusion to the mother. Symbols as in fig. 1.

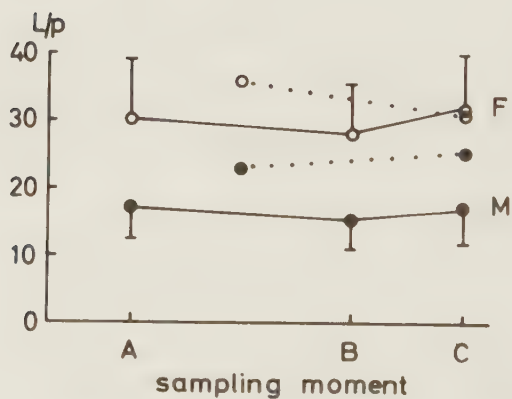


Fig 4. Maternal and fetal plasma lactate/pyruvate ratio in relation to glucose infusion to the mother. Symbols as in fig. 1.

utes after the end of the infusion, the fetal pyruvate was at the same level (0.15 mmol/l). There was a positive correlation between the fetal and the maternal plasma pyruvate concentration at each of the three observation moments ( $r = 0.67, 0.60, \text{ and } 0.87$ ).

Lactate/pyruvate (L/P) ratio (Fig. 4). Both the maternal and the fetal L/P ratio remained stable during the course of the study. Assuming the components of the LDH reaction to be at equilibrium and the L/P ratio of the extra (e) and intra (i) cellular space to be approximately equal, the following equation will be valid:

$$\frac{[L]_e}{[P]_e} \sim \frac{[L]_i}{[P]_i} = K \cdot [H^+]_i \frac{[NADH]}{[NAD^+]}$$

Also assuming that the redox state of the NADH/NAD<sup>+</sup> system is equal in the mother and in the fetus, the relation between the L/P ratio at pH 7.45 (maternal) and at pH 7.32 (fetal), those being the initial pH-values found

in the study, would be  $\frac{10^{-7.45}}{10^{-7.37}} = 0.7$ . The actual maternal and fetal L/P

ratio values obtained immediately before the glucose infusion were 17 and 30, respectively (one extreme maternal value of 95 being excluded), thus the relation between the actual maternal and fetal L/P ratio was 0.6. This agreement between theoretically calculated value and the found value suggests that the NADH/NAD<sup>+</sup> ratio is equal, or approximately equal, in mother and fetus during normal labour. The same conclusion was found to be valid from calculations of corresponding values at the end of the glucose infusion and 30 min after the infusion.

#### β-hydroxybutyrate (β-HB)

β-HB (Fig. 5). The maternal β-HB-value decreased considerably during the glucose infusion from 0.72 mmol/l to 0.16 mmol/l ( $p < 0.01$ ). In the next thirty minutes, the β-HB-level remained fairly constant (0.21 mmol/l). The initial fetal β-HB-plasma concentration (0.20 mmol/l) was lower than the maternal value and also showed a decrease during the course of glucose administration to 0.10 mmol/l ( $p < 0.01$ ); it was still at this level thirty minutes after the glucose administration. The correlation between the maternal and the fetal β-HB levels was very strong at all three sampling moments,  $r$  being 0.95, 0.82, and 0.90, respectively.

Glycerol (Fig. 6). The maternal plasma glycerol concentration exceeded the fetal corresponding value markedly throughout the study. The initial maternal level (0.146 mmol/l) decreased during the glucose infusion to 0.100 mmol/l ( $p < 0.01$ ). No changes in the maternal glycerol concentra-



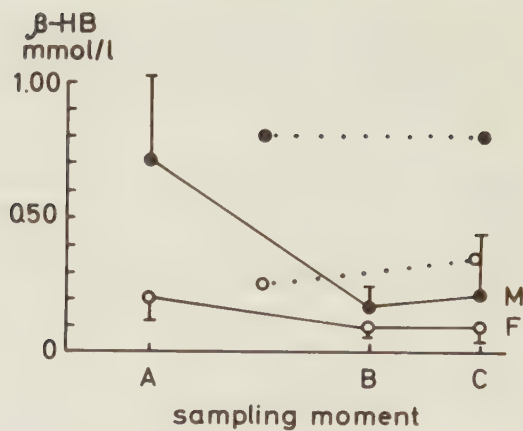


Fig 5. Maternal and fetal plasma  $\beta$ -hydroxybutyrate concentrations in relation to glucose infusion to the mother. Symbols as in fig. 1.

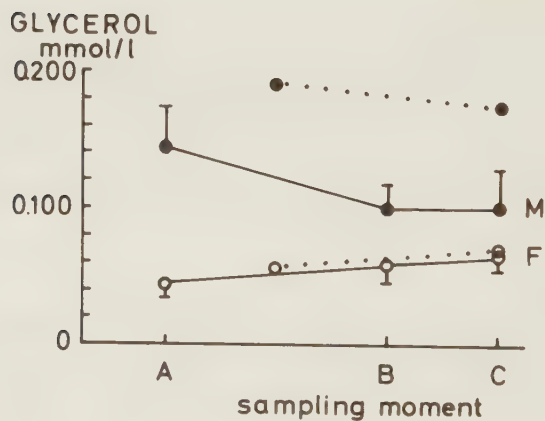


Fig 6. Maternal and fetal plasma glycerol concentrations in relation to glucose infusion to the mother. Symbols as in fig. 1.

tion occurred during the next thirty minutes. The fetal glycerol concentration was 0.043 mmol/l before the infusion. In contrast to the maternal changes, the fetal glycerol concentration increased moderately to 0.059 mmol/l ( $p < 0.05$ ) during the glucose infusion. Thirty minutes after the infusion ended, the fetal glycerol was 0.064 mmol/l, which differed from the initial fetal glycerol level ( $p < 0.01$ ). There was no correlation between maternal and fetal glycerol concentration at any of the sampling moments.

pH (Fig. 7). Very small changes were seen in the acid-base balance during this study. The maternal pH value was 7.45 before, 7.46 at the end of, and 7.47 thirty minutes after the glucose administration. Before the infusion, the fetal pH value was 7.32, and 7.30 at the end of and thirty minutes after the infusion. The maternal-fetal pH-difference increased slightly during the study from the initial value of 0.13 pH units to 0.16 pH units at the end of the infusion and 0.17 pH units thirty minutes later. The increase in the individual maternal-fetal pH-difference from before to 30 min after the end of the infusion was statistically significant ( $p < 0.05$ ).

Pco<sub>2</sub> (Fig. 8). No significant changes were observed in the maternal Pco<sub>2</sub> during the study. The maternal Pco<sub>2</sub> values were 28 mm Hg before, 25.6 mm Hg at the end of, and 24.8 mm Hg thirty minutes after the infusion. An increase in the initial fetal Pco<sub>2</sub> value from 43 to 48 mm Hg during the infusion was noted, but this increase was not statistically significant. Thirty minutes after the infusion, the fetal Pco<sub>2</sub> value had dropped to 45 mm Hg ( $p < 0.05$ ).

BD<sub>ECF</sub> (Fig. 9). During the study, the maternal BD<sub>ECF</sub>-value remained fairly constant at levels higher than the fetal values. The maternal value was 4.1 before, 5.5 at the end of, and 5.6 mmol/l thirty minutes after the infusion. A slight, but not significant, decrease in the fetal BD<sub>ECF</sub> values could be noted during the infusion, from the initial value of 3.5 mmol/l to 2.4 mmol/l. A significant rise ( $p < 0.05$ ) to 3.8 mmol/l was noted thirty minutes after the glucose administration.

Insulin (Fig. 10). The maternal plasma insulin was followed in 8 parturients and reacted to glucose infusion with an rapid early response. The maternal plasma insulin rose promptly from the basal level of 45  $\mu$ U/ml to 112  $\mu$ U/ml after 3 min of glucose infusion, and a peak (118-120  $\mu$ U/ml) was attained between 5 and 10 min, followed by a small decrease at 15 min. Subsequently the plasma insulin values remained at a steady level around 120  $\mu$ U/ml. Fifteen min after the cessation of the glucose infusion, the insulin level had decreased to 98  $\mu$ U/ml.

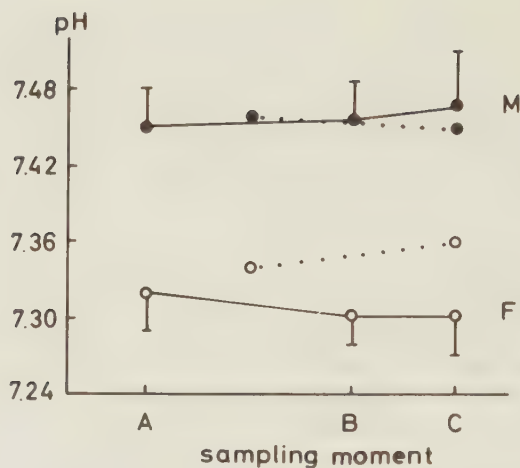


Fig 7. Maternal and fetal pH in relation to glucose infusion to the mother. Symbols as in fig. 1.

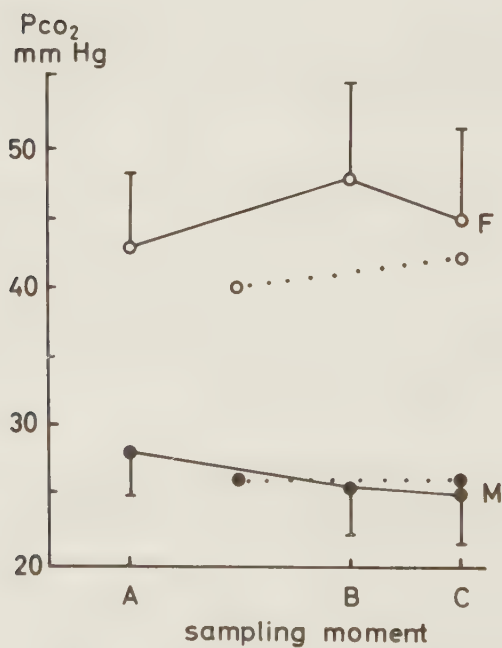


Fig 8. Maternal and fetal  $P_{CO_2}$  in relation to glucose infusion to the mother. Symbols as in fig. 1.

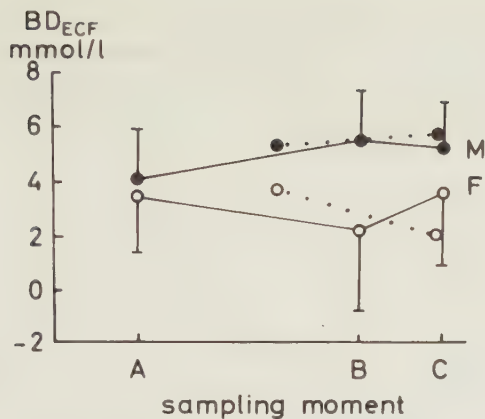


Fig 9. Maternal and fetal  $BD_{ECF}$  in relation to glucose infusion to the mother. Symbols as in fig. 1.

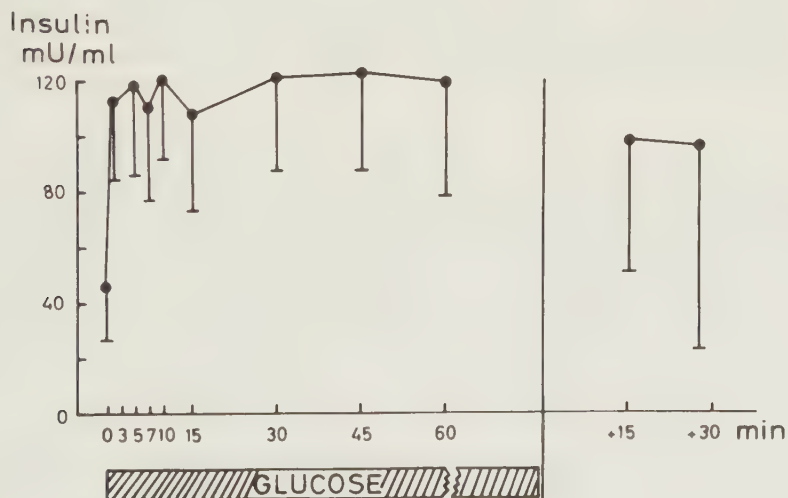


Fig 10. Maternal response of plasma insulin concentration to intravenous glucose infusion during the first stage of labour.  
Mean values and the lower 95 % confidence limits of the means.

An estimate of the Early Insulin Response (see Material and Methods) was performed (Table I). The mean early insulin response calculated from determinations at zero time and 5, 7, and 10 min after the start of glucose infusion was 138  $\mu$ U/ml with a range from 71 to 238  $\mu$ U/ml.

## DISCUSSION

In the present investigation, glucose was infused to healthy parturients during the first stage of spontaneous labour, and the simultaneous effect in maternal and fetal blood on carbohydrate, lipid, and acid-base parameters, and also the maternal insulin response were followed during a period of relative steady-state conditions during labour. The representativity of capillary blood obtained from the fetal scalp by the technique of Saling (1962) for the composition of fetal systemic blood has earlier been demonstrated for acid-base values (Gare *et al.*, 1967; Adamsons *et al.*, 1968; Teramo, 1969) and for glucose, lactate, and pyruvate (Yoshicka and Roux, 1970). The consistent pattern of the parameters found in the scalp blood in the present study provides further evidence for the validity of these sampling methods.

The administration of hypertonic fluid to pregnant women might cause an altered distribution of water and electrolytes in the extracellular space of both mother and fetus (Battaglia *et al.*, 1960), influencing the concentration of plasma constituents. No significant change of haemoglobin and sodium plasma concentrations in mother and fetus occurred during the glucose infusion, suggesting constant plasma volumes and extracellular water concentrations throughout the study. This constancy may be attributed to the relatively low rate of infusion (average 4.6 mmoles glucose/min) and the rapid passage of glucose into the intracellular space.

**Glucose and Insulin.** The maternal and fetal glucose concentrations were strongly correlated to each other during the shifts caused by the maternal glucose infusion. The maternal-fetal glucose difference increased significantly during the maternal hyperglycaemia in accordance with earlier observations (Paterson, Phillips and Wood 1967; Cordero and Anderson, 1970; Oakley, Beard and Turner, 1972). This augmentation of the maternal-fetal difference might be attributed to several factors, including saturation of the transport mechanism believed to be responsible for the transplacental glucose transfer (Widdas, 1952; Holmberg *et al.*, 1956; Ely, 1966), increased glucose consumption in the placenta, and variations of the placental regional maternal-fetal flow ratio influencing the glucose



diffusion across the exchange membranes (see discussion in Gennser and Nilsson, 1971). The fetal plasma insulin rise observed 60 min after a glucose load (Milner and Hales, 1965; Tobin, Roux and Soeldner, 1969; Coltart, Beard and Turner, 1969) implies a further explanatory factor of increased maternal-fetal glucose difference.

The initial mean plasma insulin level in the parturients in the present study exceeds the basal insulin levels in non-pregnant adults determined at the same laboratory (Thorell *et al.*, 1973). This difference might be due to the fact that the studied parturients were not in a fasting state and to the increase in basal plasma insulin levels observed during late pregnancy (Spellacy and Goetz 1963; Bleicher, O'Sullivan and Freinkel, 1964).

The insulin response to the constant glucose infusion in the women during labour was biphasic with an early response of 15 min duration followed by a steady plasma insulin level. The average pattern of plasma insulin changes in the present study is compatible with those reported for normal subjects in a non-pregnant state (Cerasi and Luft, 1967; Thorell, Nosslin and Sterky, 1973). The peak plasma insulin level during the early response in the parturients is higher than that found in non-pregnant adults (Trayner *et al.*, 1967; Thorell, Nosslin and Sterky, 1973), which agrees with the finding that glucose stimulates to greater elevations of plasma insulin during the third trimester than post partum (Bleicher, O'Sullivan and Freinkel, 1964; Spellacy *et al.*, 1965).

Alpha-adrenergic receptor stimulating agents, surgical interventions, and trauma are factors known to inhibit glucose-stimulated insulin release (see Porte and Bagdade, 1970) primarily from the acutely releasable pool. The presence of an evident early response of insulin to glucose infusion in women during the first stage of labour suggests that the stress exerted by this part of normal delivery is not sufficient to block the insulin release.

Acid-base status and glycolysis. No main changes were noted in the acid-base balance of the fetal and the maternal blood after the glucose infusion to the mother; this agrees with the result reported by Anderson, Cordero and Hon (1970). The small fluctuations of the single acid-base components were all within the normal range during spontaneous labour (Jacobson 1970). However, a slight but statistically significant increase in the maternal-fetal pH difference to 0.17 pH units had occurred 30 min after the glucose infusion compared with the value before the glucose was administered and thus deserves a brief comment. A maternal-fetal pH difference exceeding 0.20 pH units may be regarded as an indication of fetal acidosis, as earlier reported (Heinrich *et al.*, 1972; Rooth, McBride and Ivy, 1973; Gårdmark, Jacobson and Rooth, 1974) and values between 0.15 and 0.19 pH units might be considered as borderline values

requiring further observation. The increase in the maternal-fetal pH difference found is ascribable to a slight simultaneous increase in maternal pH and decrease in fetal pH; these changes per se being within the ordinary range in normal untreated delivery cases. Furthermore, the maternal-fetal pH difference should be regarded in relation to the somewhat high pH difference, 0.13 pH units, existing already before the glucose was administered.

The rise of maternal pyruvate concentration after glucose administration might be regarded as a consequence of an increased glycolysis caused by the high availability of glucose. In the lactate-forming reaction, the relation between pyruvate and lactate concentration is pH-dependent, and at a constant pH, an increase in the pyruvate concentration will therefore lead to a secondary increase in the lactate concentration, as pointed out by Huckabee (1958). As no changes in the extracellular pH and in the lactate/pyruvate ratio were found in the present study during and after the glucose load, the maternal lactate increase must be considered secondary to the pyruvate rise. The simultaneous increase in the fetal pyruvate and lactate concentration might be similarly explained as secondary to the rise in the fetal plasma glucose. The numerical relation between the fetal and maternal lactate/pyruvate ratio found in the present investigation agrees well with the theoretically expected value, as the lactate/pyruvate ratio is pH dependent (cf. also Folbergrova, Mac Millan and Siesjö, 1972). High lactate concentration after glucose administration to the mother has also been observed in human prematures (Šabata *et al.*, 1967), in chronically catheterized fetal lambs without simultaneous maternal lactate rise (Shelley, 1973), and in newborns exposed to cold (Soltész *et al.*, 1971). It has therefore been suggested that the use of prenatal glucose administration might involve a risk of increased fetal or neonatal acidosis in cases of hypoxia (Shelley, 1973). The constancy of the lactate/pyruvate ratio, pH, and  $BD_{ECF}$  in both mother and fetus makes it evident that the glucose administration per se does not normally induce acidosis in the fetus, which is in accordance with the findings of Anderson, Cordero and Hon (1970). However, it should be noted in this context that the maternal-fetal pH difference showed a moderate tendency to rise up to or above 0.15 pH units. The clinical validity of this is uncertain as is the effect of maternal glucose infusion on the fetal biochemistry in cases of fetal distress, which deserves further investigations.

**Lipid metabolism.** An increase of lipid mobilization in fasting women during the later part of pregnancy has been reported (Bleicher, O'Sullivan and Freinkel, 1964), and a correlation between the delivery time and the maternal  $\beta$ -HB-concentration was found by Persson and Thunell (1971) and Paterson *et al.* (1967). On the other hand, women with a normal caloric intake during the last trimester had no signs of lipid

mobilization (Persson, 1974). Thus the initially high glycerol and  $\beta$ -HB-levels in this study suggest that the women, despite being allowed rather unrestricted caloric intake, are actually in caloric imbalance during labour. This presumption is strengthened by the observation that glucose administration to the mother resulted in a marked decrease in the maternal  $\beta$ -HB and glycerol concentrations, indicating a reduction of lipid mobilization. After glucose infusion during delivery, a similar fall of maternal ketone bodies was reported by Paterson *et al.* (1967), and of maternal glycerol by Šabata, Wolf and Lausmann (1970).

A strong correlation between fetal and maternal plasma  $\beta$ -HB concentration was found in accordance with earlier reports (Šabata, Wolf and Lausmann, 1968). An umbilical arterio-venous difference of  $\beta$ -HB has been found in normal deliveries (Šabata, Wolf and Lausmann, 1968; Persson and Thunell, 1971; Gårdmark, Jacobson and Rooth, 1974 b), suggesting a net fetal uptake of this ketone body, this being supported by the initially high maternal-fetal concentration gradient in this study. However, the possibility of a slow placental transfer as a cause of this gradient must also be taken into account.

Opinions differ about the transplacental passage of glycerol. Umbilical glycerol values have been reported with no significant arterio-venous difference (Šabata, Wolf and Lausmann, 1968; Persson and Thunell, 1971) or with the venous concentration significantly exceeding the arterial (Sheath *et al.*, 1972; Gårdmark, Jacobson and Rooth, 1974 b). For comparison, it should be noted that the fate of fetal free fatty acids after glucose administration to the mother is equally unclear in reports with conflicting results (Roux and Romney, 1967; Šabata, Wolf and Lausmann, 1968; Tobin, Roux and Soeldner, 1969). The observation in this study that the maternal and fetal glycerol levels vary independently suggests that the glycerol transfer through the placenta, if present, is of low magnitude.

A small but statistically significant increase in glycerol in fetal plasma was noted during the glucose infusion to the mother. Theoretically, this rise in fetal glycerol might be ascribed to an augmentation of glycerol synthesis via the increased glycolytic activity. However, fetuses of parturients not receiving glucose display a similar increase in plasma glycerol during labour (Gårdmark, Jacobson and Rooth, 1974 a, b), suggesting that a catecholamine induced lipid mobilization secondary to the stress of labour is at least partly responsible for the rising fetal glycerol level in the present series.

The significance of the fetal glycerol rise is strengthened by the fact that it occurs without a simultaneous increase in the maternal glycerol level and in both normal and high fetal plasma glucose levels. A rapid increase

in lipid metabolism occurs during the first 24 hours of extrauterine life (see Persson and Thunell, 1971), and the observed fetal glycerol increase during labour suggests a fetal ability of lipid mobilization already before birth.

## SUMMARY

- (1) 13 parturients during normal labour were given intravenous glucose infusion, elevating plasma glucose to a steady level. Glucose, lactate, pyruvate,  $\beta$ -hydroxybutyrate, glycerol, and acid-base components were determined in samples obtained simultaneously from maternal venous and fetal capillary blood before, at the end of, and 30 min after the glucose load. Maternal insulin was assayed in 8 cases.
- (2) The maternal-fetal difference of plasma glucose increased with increasing maternal plasma glucose level; glucose load caused a rapid early response of maternal insulin release.
- (3) A parallel rise in plasma lactate and pyruvate occurred in both fetus and mother after the glucose infusion; no major disturbances of the fetal acid-base balance were found.
- (4) The basal maternal  $\beta$ -hydroxybutyrate and glycerol concentrations decreased significantly during glucose load, suggesting negative caloric balance in normal parturients during early labour. The study demonstrated that, at term, components of lipid metabolism in fetal and maternal plasma - in contrast to glucose - vary independently. A small but significant rise in fetal plasma glycerol, irrespective of glucose level, suggests a fetal lipid mobilization already antenatally.
- (5) The present study does not permit any conclusions regarding metabolic consequences for the fetus of glucose infusion to the mother in cases of intrauterine distress.

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FETAL AND MATERNAL ACID-BASE BALANCE AND GLUCOSE  
METABOLISM DURING LABOUR IN BREECH PRESENTATION

Stig Gårdmark, Lennart Jacobson & Gösta Rooth





More than ten years have elapsed since Saling (1962) introduced his technique of fetal blood sampling during labour. Compared with the extensive number of investigations published on fetal scalp blood, only few reports have appeared on fetal blood sampled in breech presentation. Kubli (1966) reported on the fetal acid-base status in 5 cases, and Eliot & Hill (1972) and Hill & Eliot (1973) investigated fetal pH in a series of approximately 80 breech deliveries. It would thus be of interest to investigate on a broader basis the composition of fetal blood sampled during labour from the presenting breech (including the relation between fetal and maternal blood composition), and to evaluate the applicability of the fetal blood sampling method as a routine in such cases.

For that purpose we determined acid-base components, oxygen saturation, lactate, pyruvate, and glucose in fetal blood sampled repeatedly during labour in a series of uncomplicated breech or breech-foot deliveries. The results were compared with those found in a series of clinically normal cases of vertex presentation. Three cases of breech delivery with clinical signs of moderate fetal distress were also included in the study. In all cases, the composition of the fetal blood was compared with that of the maternal blood, simultaneously sampled.

## MATERIAL AND METHODS

The series comprises 18 unselected breech or breech-foot delivery cases. The age of the mothers ranged from 17 to 34 years (mean 24.8 years). Fourteen of the parturients were primiparae and four were multiparae. Fifteen were in all respects obstetrically normal, and their infants had a one-minute Apgar score of 8-10. The remaining three were classified as moderate fetal distress on the basis of a one-minute Apgar score of 5-7. The birth weight of the infants ranged from 2,500 g to 4,820 g (mean 3,284 g). The only obstetrical interventions occasionally performed at delivery were pudendal block and release of the arms by means of the Løvset manoeuvre. In all cases, the aftercoming head was delivered by the Bracht manoeuvre. A prophylactic episiotomy was generally applied.

The control series comprises 16 primiparae and their fetuses, spontaneously delivered in the occiput anterior presentation. This group, which fulfils high criteria of clinical normality, was primarily intended for other purposes but well suitable in this context as the cases were analysed in the same way and during the same period of time as the breech series. The age of these mothers ranged from 17 to 32 years (mean 23.1 years).

All infants of this series had a one-minute Apgar score of 8-10. The birth weights ranged from 2,680 to 4,370 g (mean 3,504 g).

As there are systematic changes in the maternal and fetal blood composition in the course of labour, samples from different cases should only be compared if taken at equivalent stages of labour. The reference system, previously defined by Jacobson (1970) by which the course of labour is divided into sampling periods (1-8), was therefore used. In the subsequent presentation, the results from the sampling periods 1-4 (= 1<sup>st</sup> stage of labour), periods 5-6 (= early and middle phase of 2<sup>nd</sup> stage), and for some parameters also the periods 7-8 (= last 15 minutes of 2<sup>nd</sup> stage) were pooled.

Fetal blood sampling was routinely made through an amnioscope even at the end of the second stage, in order to eliminate any contamination with maternal blood, amniotic fluid, and urine. Disposable blades, manufactured by Eschmann Ltd., England, were used for the skin incision. The construction of the blades ensures an incision depth of not more than 2-3 mm. The blood was anaerobically collected in heparinized glass capillaries approximately 20 cm in length and connected in their outer end with a polyethylene catheter to facilitate light suction if necessary. Maternal blood was sampled from the finger tip after warming the hand in hot water for some minutes. At the delivery, the umbilical cord was clamped before the first breath, and blood from the artery and vein was anaerobically drawn into heparinized glass syringes.

In order not to influence the clinical management of the deliveries according to the established routine of the department, the obstetrician-in-charge at the delivery ward was not informed of the results of the blood analyses.

The following parameters were determined: pH,  $P_{CO_2}$ , Base Deficit, oxygen saturation ( $SO_2$ ), plasma lactate, pyruvate, and glucose.

pH was measured by means of the Radiometer glass microelectrode unit E 5021 and pH meter PHM 27.  $P_{CO_2}$  was determined with the Eschweiler micro- $CO_2$ -electrode assembly. Base Deficit was calculated for the extracellular fluid compartment ( $BD_{ECF}$ ) from the Siggaard-Andersen alignment nomogram (1963), read at the Hb 5 g/100 ml-line.  $SO_2$  was measured by means of the photometric micro-method devised by Siggaard-Andersen, Jørgensen & Naeraa (1962).

For glucose, lactate, and pyruvate determinations, the samples were collected into micro-tubes and immediately centrifuged in a Beckman high speed microcentrifuge. The plasma was separated and stored in a deep freeze for later analysis. The determinations were made with ultramicro-

adaptations of the Boehringer enzymatic methods; colorimetric procedure was used for glucose, spectrophotometric procedure for lactate, and fluorometric procedure for pyruvate.

## RESULTS

### I. SERIES OF NORMAL BREECH DELIVERIES

pH. The mean values of pH found at different sampling periods during labour in the breech delivery series and in the control series are given in Tables I and II, and illustrated in Fig. 1. During the major course of labour, the mean pH in fetal and in maternal blood were almost identical in the two series. Fetal as well as maternal blood pH tended to decrease during labour, the decrease being statistically significant for fetal pH in both series ( $p < 0.01$ ), but for maternal blood only in the control series ( $p < 0.05$ ).

At the end of labour (from sampling period 7, i. e. 15–5 minutes before birth), the fetal pH decreased somewhat more in the series of breech presentation than in the control group. Consequently, the maternal-fetal difference ( $\Delta$  pH) became greater in the former series at the terminal phase of labour. As the mean values show (Tables I and II),  $\Delta$  pH was 0.21 pH units in the breech delivery group and 0.13 pH units in the control group at sampling period 8 (i. e.  $\leq 5$  minutes before birth). When calculated on the basis of paired samples, the mean  $\Delta$  pH values were found to be 0.18 and 0.14 pH units, respectively. In the first stage of labour, the mean of individual  $\Delta$  pH was 0.11 in the breech delivery series and 0.12 in the control group. The  $\Delta$  pH increase of 0.07 pH units during labour in the breech delivery series was statistically significant ( $p < 0.01$ ).

In both series, the pH mean value in fetal blood at sampling period 8 fell between the mean levels of pH in umbilical venous and in arterial blood.

Pco<sub>2</sub>. (Tables I and II, Fig. 2). No statistically significant differences were found between the two series in the mean level of Pco<sub>2</sub> throughout labour in maternal and in fetal blood, respectively.

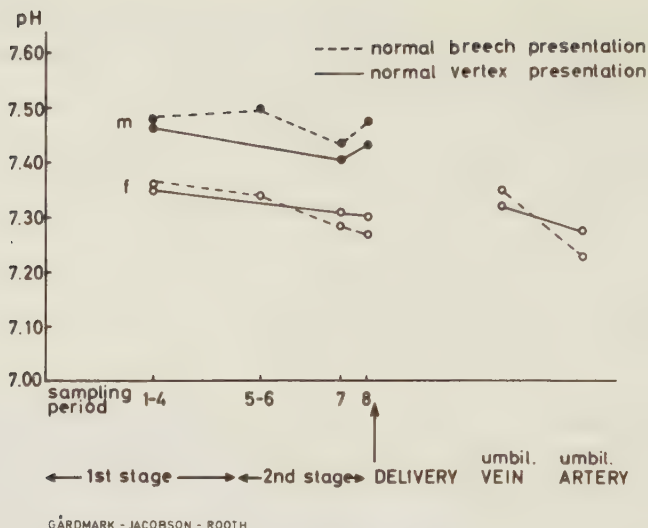


Fig 1. pH mean in maternal<sup>(m)</sup> and fetal<sup>(f)</sup> blood at different periods during labour in the breech series and in the control series

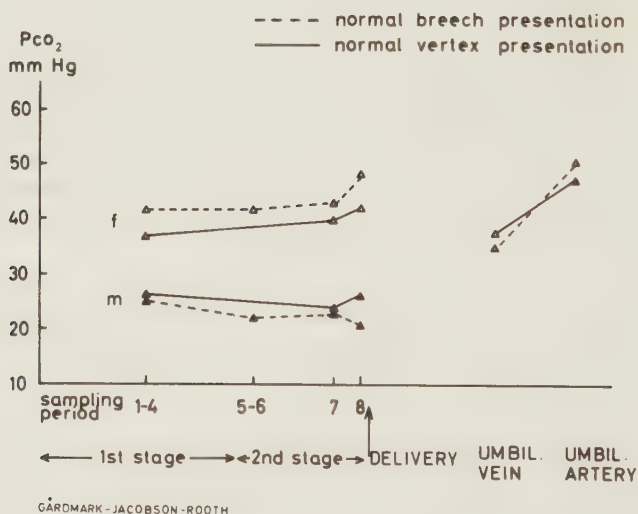


Fig 2. Pco<sub>2</sub> mean in maternal<sup>(m)</sup> and fetal<sup>(f)</sup> blood at different periods during labour in the breech series and in the control series

Table I. Different maternal (M) and fetal (F) blood components, determined in different stages of labour and in cord blood in the series of breech deliveries. Mean values, standard deviations and 95 % confidence limits of the means.

|                         | 1st stage |           |            | Early and middle 2nd stage |           |            | Late 2nd stage      |           |            | Umbilical vessels |           |            |
|-------------------------|-----------|-----------|------------|----------------------------|-----------|------------|---------------------|-----------|------------|-------------------|-----------|------------|
|                         | n         | $\bar{x}$ | ±95% c.lim | n                          | $\bar{x}$ | ±95% c.lim | n                   | $\bar{x}$ | ±95% c.lim | n                 | $\bar{x}$ | ±95% c.lim |
| pH                      | M 13      | 7.47      | 0.04       | 5                          | 7.50      | 0.08       | 4                   | 7.44      | 0.02       | 9                 | 7.48      | 0.06       |
|                         | F 13      | 7.36      | 0.02       | 5                          | 7.34      | 0.04       | 8                   | 7.28      | 0.07       | 12                | 7.27      | 0.06       |
|                         |           | ±0.02     |            |                            | ±0.04     |            |                     | ±0.06     |            |                   | ±0.04     |            |
| Pco <sub>2</sub>        | M 12      | 25.4      | 5.3        | 5                          | 22.0      | 4.9        | 3                   | 23.3      | 4.0        | 9                 | 21.2      | 5.9        |
|                         |           | ± 3.3     |            |                            | ± 6.1     |            |                     | ± 9.9     |            |                   | ± 4.6     |            |
| mm Hg                   | F 12      | 41.7      | 6.9        | 5                          | 41.8      | 10.6       | 7                   | 42.8      | 10.9       | 10                | 48.3      | 16.6       |
|                         |           | ± 4.4     |            |                            | ±13.0     |            |                     | ±10.0     |            |                   | ±12.0     |            |
| BDECF                   | M 12      | 4.4       | 3.1        | 5                          | 5.8       | 3.1        | 3                   | 7.3       | 2.1        | 9                 | 7.7       | 3.0        |
|                         |           | ± 1.9     |            |                            | ± 3.9     |            |                     | ± 5.2     |            |                   | ± 2.3     |            |
| mmol/l                  | F 12      | 1.6       | 4.0        | 5                          | 3.0       | 5.0        | 7                   | 5.6       | 5.9        | 10                | 4.3       | 5.6        |
|                         |           | ± 2.6     |            |                            | ± 6.4     |            |                     | ± 6.2     |            |                   | ± 4.1     |            |
| Glucose mg%             | M 11      | 102       | 21         | 4                          | 114       | 10         | Sampling period 7-8 |           |            | 10                | 125       | 29         |
|                         |           | ± 14      |            |                            | ± 15      |            |                     |           |            |                   | ± 21      |            |
|                         | F 11      | 75        | 13         | 4                          | 82        | 12         |                     |           |            | 11                | 88        | 15         |
|                         |           | ± 9       |            |                            | ± 19      |            | Sampling period 7-8 |           |            |                   | ± 10      |            |
| Lactate mmol/l          | M 11      | 2.5       | 0.6        | 4                          | 3.6       | 1.1        |                     |           |            | 10                | 5.5       | 1.6        |
|                         |           | ± 0.4     |            |                            | ± 1.7     |            |                     |           |            |                   | ± 1.2     |            |
|                         | F 11      | 2.4       | 0.4        | 4                          | 3.5       | 0.9        | Sampling period 7-8 |           |            | 11                | 5.6       | 1.8        |
|                         |           | ± 0.3     |            |                            | ± 1.4     |            |                     |           |            |                   | ± 1.2     |            |
|                         | M 11      | 0.13      | 0.05       | 4                          | 0.18      | 0.02       |                     |           |            | 10                | 0.20      | 0.07       |
|                         |           | ± 0.03    |            |                            | ± 0.03    |            | Sampling period 7-8 |           |            |                   | ± 0.05    |            |
| Pyruvate mmol/l         | F 11      | 0.11      | 0.04       | 4                          | 0.15      | 0.05       |                     |           |            | 11                | 0.14      | 0.04       |
|                         |           | ± 0.02    |            |                            | ± 0.07    |            |                     |           |            |                   | ± 0.03    |            |
| SaO <sub>2</sub> % sat. | F 13      | 61        | 12         | 5                          | 50        | 11         | 6                   | 45        | 13         | 11                | 47        | 15         |
|                         |           | ± 7       |            |                            | ±13       |            |                     | ±14       |            |                   | ±10       |            |
|                         |           |           |            |                            |           |            |                     |           |            | V 13              | 76        | 20         |
|                         |           |           |            |                            |           |            |                     |           |            | A                 | ±12       |            |
|                         |           |           |            |                            |           |            |                     |           |            | A                 | 12        | 43         |
|                         |           |           |            |                            |           |            |                     |           |            |                   | ±10       |            |
|                         |           |           |            |                            |           |            |                     |           |            |                   | ±10       |            |



Table II. Different maternal (M) and fetal (F) blood components, determined in different stages of labour and in cord blood in the control series of normal deliveries in vertex presentation.  
Mean values, standard deviations and 95 % confidence limits of the means.

|                             | 1st stage           |                            |      | Late 2nd stage         |                            |      | Umbilical vessels |                            |      |
|-----------------------------|---------------------|----------------------------|------|------------------------|----------------------------|------|-------------------|----------------------------|------|
|                             | Sampling period 1-4 |                            |      | Sampling period 7      |                            |      | Sampling period 8 |                            |      |
|                             | n                   | $\bar{x}$<br>±95%<br>c.lim | sd   | n                      | $\bar{x}$<br>±95%<br>c.lim | sd   | n                 | $\bar{x}$<br>±95%<br>c.lim | sd   |
| pH                          |                     |                            |      |                        |                            |      |                   |                            |      |
| M                           | 17                  | 7.46<br>±0.02              | 0.04 | 5                      | 7.41<br>±0.05              | 0.04 | 11                | 7.43<br>±0.02              | 0.03 |
| F                           | 17                  | 7.35<br>±0.02              | 0.03 | 5                      | 7.31<br>±0.06              | 0.05 | 10                | 7.30<br>±0.05              | 0.07 |
| Pco <sub>2</sub><br>mm Hg   |                     |                            |      |                        |                            |      |                   |                            |      |
| M                           | 17                  | 26.7<br>±2.3               | 4.5  | 5                      | 23.9<br>±4.1               | 3.3  | 11                | 25.6<br>±2.0               | 3.0  |
| F                           | 17                  | 36.9<br>±2.4               | 4.8  | 4                      | 40.1<br>±12.2              | 7.7  | 11                | 42.2<br>±5.6               | 8.6  |
| BD <sub>ECF</sub><br>mmol/l |                     |                            |      |                        |                            |      |                   |                            |      |
| M                           | 17                  | 4.4<br>±1.5                | 2.9  | 5                      | 8.7<br>±4.8                | 3.9  | 11                | 6.9<br>±1.8                | 2.7  |
| F                           | 17                  | 4.8<br>±1.6                | 3.2  | 4                      | 4.6<br>±1.7                | 1.0  | 11                | 5.3<br>±2.6                | 3.9  |
| Glucose<br>mg%              |                     |                            |      |                        |                            |      |                   |                            |      |
| M                           | 14                  | 93<br>±8                   | 14.6 | Sampling<br>period 7-8 |                            |      | 13                | 125<br>±18                 | 30.1 |
| F                           | 14                  | 79<br>±8                   | 14.2 |                        |                            |      | 10                | 91<br>±14                  | 20.2 |
| Lactate<br>mmol/l           |                     |                            |      |                        |                            |      |                   |                            |      |
| M                           | 10                  | 4.2<br>±2.6                | 3.6  |                        |                            |      | 10                | 7.0<br>±1.5                | 2.2  |
| F                           | 10                  | 4.0<br>±1.1                | 1.5  |                        |                            |      | 8                 | 4.9<br>±1.8                | 2.2  |
| Pyruvate<br>mmol/l          |                     |                            |      |                        |                            |      |                   |                            |      |
| M                           | 11                  | 0.16<br>±0.07              | 0.10 |                        |                            |      | 12                | 0.27<br>±0.07              | 0.11 |
| F                           | 13                  | 0.14<br>±0.04              | 0.07 |                        |                            |      | 10                | 0.17<br>±0.06              | 0.08 |
|                             |                     |                            |      |                        |                            |      | 10                | 0.21<br>±0.08              | 0.10 |
|                             |                     |                            |      |                        |                            |      | 10                | 0.22<br>±0.07              | 0.10 |

The  $P_{CO_2}$  of maternal blood did not change during the course of labour in either of the two series. As Fig. 2 shows, the mothers of the breech delivery series tended to hyperventilate slightly more than did the mothers of the control group (cf. the corresponding small maternal pH difference between the series in Fig. 1).

In the fetal blood, the  $P_{CO_2}$  mean became somewhat higher at the end of labour in the breech presentation series than in the control series. The difference is not statistically significant. The mean value of fetal  $P_{CO_2}$  immediately before birth in the breech delivery series lay closer to the  $P_{CO_2}$  mean found in umbilical arterial blood than to the  $P_{CO_2}$  in the umbilical venous blood.

No statistical differences were found between corresponding  $P_{CO_2}$  means of the umbilical cord blood in the two series.

$BD_{ECF}$ . (Tables I and II, Fig. 3). Throughout labour, there was no difference between the two series in maternal  $BD_{ECF}$  mean levels. In both series, the maternal blood  $BD_{ECF}$  was moderately, but significantly, increased during labour ( $p < 0.01$  for both series, calculated from the values of individual  $BD_{ECF}$  changes).

In fetal blood, the mean level of  $BD_{ECF}$  was constantly lower than the maternal  $BD_{ECF}$  level in both series; in other words, the maternal-fetal difference ( $\Delta BD_{ECF}$ ) was constantly positive, as it usually is under normal conditions. As the Tables and Fig. 3 show, the fetal  $BD_{ECF}$  mean was lower in the breech delivery series than in the control series in the first stage of labour, the difference being statistically significant ( $p < 0.05$ ). In the second stage of labour, however, no significant difference was present between the series in this respect. In the control group, the fetal  $BD_{ECF}$  level remained constant during labour, whereas in the breech delivery series, the fetal  $BD_{ECF}$  increased from the lower initial level to the level of the control group. This increase, however, is not statistically significant ( $p > 0.05$ ).

In some cases of the breech delivery series, repeated samples were drawn with very short intervals in period 8, i. e. during the most terminal phase of labour and during actual delivering of the fetal body. It was found then, as seen in Fig. 3 (sampling period 8<sub>2</sub>), that the fetal  $BD_{ECF}$  level showed an obvious tendency to rise rapidly at this final, short period before birth.

No significant differences were present between the corresponding  $BD_{ECF}$  means of the umbilical cord blood in the two series.

SaO<sub>2</sub>. (Table I, Fig. 4). Oxygen saturation of the fetal blood was systematically determined in the breech delivery series only. No statistically significant change of the mean SaO<sub>2</sub> level was found to occur during labour, although there was a tendency for the level to fall during the second stage. The numerical values of the SaO<sub>2</sub> mean at the different sampling periods as well as in umbilical cord blood agree closely with those found in a normal series of vertex presentation, previously reported by Jacobson (1970).

Lactate. (Tables I and II, Fig. 5). In the first stage of labour, the mean plasma lactate concentration of maternal and that of fetal blood in the breech delivery series were lower than corresponding means in the control series, but the difference was significant for the fetal blood lactate only ( $p < 0.01$ ). In the second stage of labour, no differences were encountered between the two series, nor were there any differences between corresponding mean values of the umbilical cord blood.

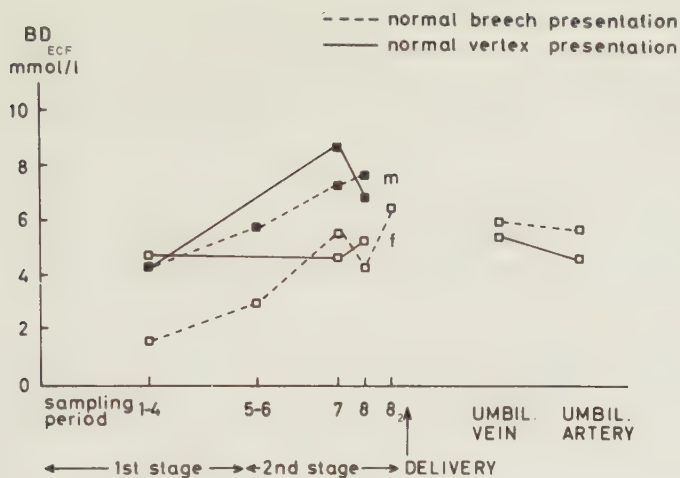
In both series, the plasma lactate concentration in maternal blood increased by approximately 3 mmol/l during the course of labour. Statistically, this increase was found to be significant for the breech delivery series ( $p < 0.001$ ), but not significant for the control series owing to a more scattered distribution of the individual values.

In fetal blood, the mean concentration of plasma lactate also increased in both series. In the control series, the increase was slight and not statistically significant. In the breech delivery series, however, the plasma lactate increased from a very low value to the level of the control series, this increase being significant ( $p < 0.001$ ) (cf. corresponding BD<sub>ECF</sub> changes above).

Pyruvate. (Tables I and II, Fig. 5). The mean levels of plasma pyruvate concentration in maternal and in fetal blood did not differ significantly between the two series during labour.

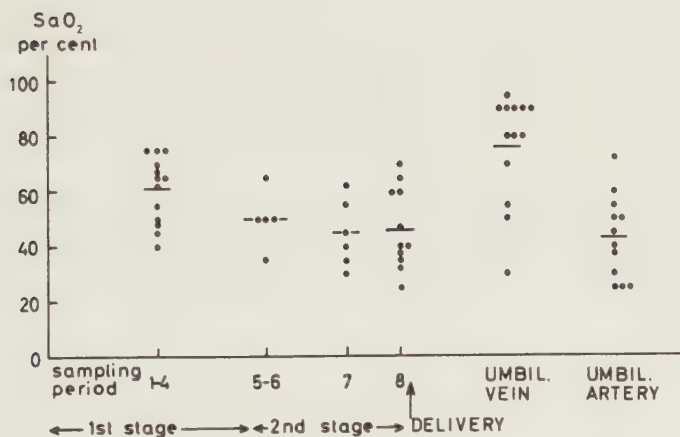
In both series, the pyruvate concentration showed a small increase during labour, the increase being somewhat more marked and statistically significant in the maternal blood ( $p < 0.05$  in both series). In the fetal blood, the pyruvate concentration increase was not statistically significant in the two series.

The mean levels of pyruvate in the cord blood did not differ between the series.



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Fig 3. BD<sub>ECF</sub> mean in maternal<sup>(m)</sup> and fetal<sup>(f)</sup> blood at different periods during labour in the breech series and in the control aeries



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Fig 4. Oxygen saturation in fetal blood at different periods during labour in the breech series

Glucose. (Tables I and II, Fig. 5). The mean values of plasma glucose in maternal and in fetal blood did not differ between the breech delivery series and the control series. In both series, throughout labour, the glucose concentration was higher in the maternal blood than in the fetal blood.

In the breech delivery series, as well as in the control series, an increase in the mean glucose concentration was found to occur in the course of labour, the increase being somewhat more pronounced in the maternal blood than in the fetal blood, but equally significant in both blood compartments ( $p < 0.05$ ).

The mean concentration of glucose was higher in the umbilical venous blood than in the arterial blood in both series. There were no significant differences between the series in umbilical cord blood glucose concentrations.

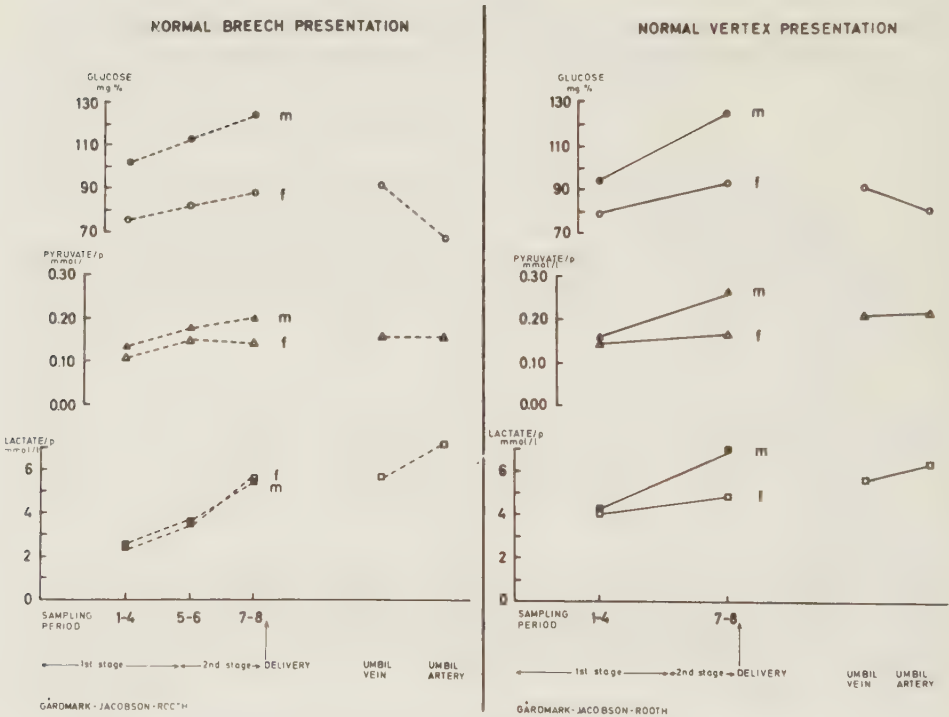


Fig 5. Mean values of glucose, pyruvate and lactate in maternal<sup>(m)</sup> and fetal<sup>(f)</sup> blood at different periods during labour in the breech series and in the control series



## II. CASES OF BREECH DELIVERY WITH FETAL DISTRESS AT BIRTH

The study includes three breech delivery cases with signs of moderate fetal depression at birth.

Case I. The obstetrical course was normal until 10 minutes before delivery (sampling period 7). At that time, the release of the stripped-up arms proved difficult and therefore time-consuming. The one-minute Apgar score was 7, but the depression of the infant was of short duration, and the 5-minute Apgar score was 9. The birth weight was 3,730 g.

Case II. From sampling period 6, in this case equal to 23 minutes before birth, fetal bradycardia of the early deceleration type was recorded. The one-minute Apgar score was 6. It increased to 8 at 10 minutes by simple resuscitation procedures. The birth weight was 2,890 g.

Case III. This was a foot presentation. No FHR disturbances were noted before birth. The infant was moderately depressed at birth, the one-minute Apgar score being 5. It increased to 10 at 10 minutes by simple resuscitation procedures. The birth weight was 3,650 g.

Table III gives the values of the different components determined in maternal, fetal, and umbilical cord blood of the three cases. Fig. 6 illustrates the fetal blood pH in the three cases in relation to the pH mean values found in the normal breech delivery series.

As Table III and Fig. 6 show, all three cases had at the end of labour a fetal pH more or less below the mean fetal pH level in the normal breech delivery series. This was also true for the values of pH in the umbilical cord blood of the cases.

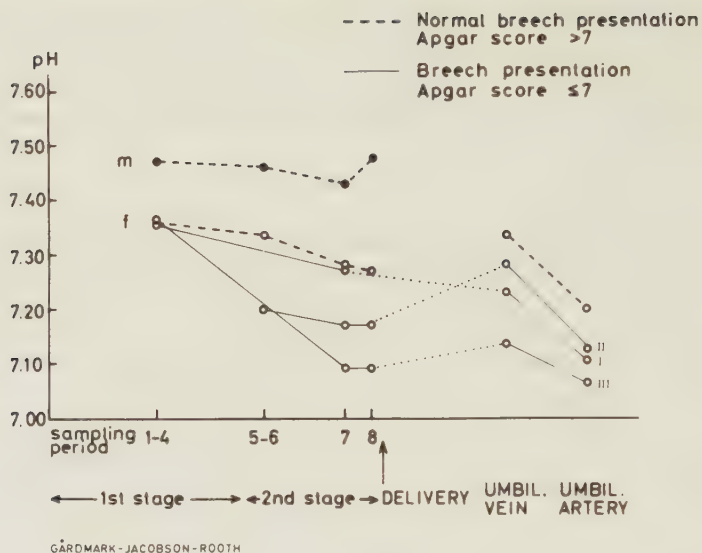


Fig 6. Fetal pH during labour in the three breech delivery cases with lowered Apgar score at birth. For comparison are given the fetal<sup>(f)</sup> and maternal<sup>(m)</sup> mean pH levels in the normal series of breech presentation

Table III. Figures for different blood components in maternal and fetal blood during labour and in umbilical cord blood at birth in three cases of breech delivery with signs of fetal distress.

|                       |   | Sampling periods |       |       |       | Umbilical cord |       |
|-----------------------|---|------------------|-------|-------|-------|----------------|-------|
|                       |   | 1-4              | 5-6   | 7     | 8     | V              | A     |
| <u>Case I</u>         |   |                  |       |       |       |                |       |
| pH                    | M | 7.44             |       | 7.39  |       | 7.23           | 7.11  |
|                       | F | 7.36             |       | 7.27  |       |                |       |
| Pco <sub>2</sub>      | M | 26.0             |       | 25.0  |       | 53.0           | 63.0  |
|                       | F | 47.0             |       | 52.0  |       |                |       |
| BD <sub>ECF</sub>     | M | 6.0              |       | 9.0   |       | 5.0            | 8.5   |
|                       | F | -1.0             |       | 3.0   |       |                |       |
| Lact. p               | M | 2.31             |       | 6.04  |       | 4.55           | -     |
|                       | F | 2.05             |       | 5.41  |       |                |       |
| Pyruvate <sub>p</sub> | M | 0.035            |       | 0.140 |       | 0.092          | -     |
|                       | F | 0.051            |       | 0.092 |       |                |       |
| SaO <sub>2</sub>      | F | 70               |       | 60    |       | 50             | -     |
| <u>Case II</u>        |   |                  |       |       |       |                |       |
| pH                    | M |                  | 7.47  | -     | 7.47  | 7.28           | 7.12  |
|                       | F |                  | 7.20  | 7.17  | 7.17  |                |       |
| Pco <sub>2</sub>      | M |                  | 19.5  | -     | 19.5  | 29.0           | 43.0  |
|                       | F |                  | 34.0  | 48.0  | 48.0  |                |       |
| BD <sub>ECF</sub>     | M |                  | 9.0   | -     | 9.0   | 12.0           | 14.0  |
|                       | F |                  | 13.0  | 10.0  | 10.0  |                |       |
| Lact. p               | M |                  | 5.61  | -     | 5.71  | 7.29           | 8.12  |
|                       | F |                  | 9.27  | -     | 9.50  |                |       |
| Pyruvate <sub>p</sub> | M |                  | 0.297 | -     | 0.268 | 0.164          | 0.199 |
|                       | F |                  | 0.202 | -     | 0.201 |                |       |
| SaO <sub>2</sub>      | F |                  | 65    |       | 45    | 85             | 50    |
| <u>Case III</u>       |   |                  |       |       |       |                |       |
| pH                    | M | 7.43             |       | 7.38  | -     | 7.14           | 7.06  |
|                       | F | 7.37             |       | 7.09  | 7.09  |                |       |
| Pco <sub>2</sub>      | M | 31.5             |       | 30.0  | -     | 64.0           | 80.0  |
|                       | F | 47.0             |       | 64.0  | 84.0  |                |       |
| BD <sub>ECF</sub>     | M | 2.5              |       | 6.5   | -     | 7.0            | 7.5   |
|                       | F | -1.5             |       | 10.0  | 5.0   |                |       |
| Lact. p               | M | 3.17             |       | 5.38  |       | 7.92           | 8.48  |
|                       | F | 2.05             |       | 8.91  |       |                |       |
| Pyruvate <sub>p</sub> | M | 0.139            |       | 0.165 |       | 0.172          | 0.176 |
|                       | F | 0.092            |       | 0.185 |       |                |       |
| SaO <sub>2</sub>      | F | 60               |       | 38    |       | 25             | 25    |

In Cases II and III, the most depressed at birth, the maternal-fetal pH difference ( $\Delta$  pH) was increased at the end of labour to 0.30 and 0.29 pH units, respectively, which should be compared with approximately 0.18 in the normal breech delivery series and approximately 0.14 pH units in the control series of vertex presentation.

The  $P_{\text{co}_2}$  of the fetal blood was substantially higher than the corresponding mean values in the normal breech delivery group in Case III at the end of labour and in umbilical cord blood in Case I.

The fetal  $\text{BD}_{\text{ECF}}$  was higher than in the normal breech series in Cases II and III during the second stage of labour. In these two cases, the fetal  $\text{BD}_{\text{ECF}}$  was higher than the maternal  $\text{BD}_{\text{ECF}}$ , leading to a negative maternal-fetal difference ( $\Delta \text{BD}_{\text{ECF}}$ ). In Case I, the fetal  $\text{BD}_{\text{ECF}}$  remained normal in the course of labour; but in the umbilical artery blood, the  $\text{BD}_{\text{ECF}}$  value exceeded the corresponding mean of the normal breech delivery series by approximately 3 mmol/l.

The fetal plasma lactate concentration in Cases II and III at the end of labour exceeded that of the normal breech delivery series by approximately 3.5 mmol/l, whereas no difference was noted between the normal series and Case I in this respect.

The fetal plasma pyruvate concentration in Cases II and III, at the end of labour, was slightly above the corresponding mean in the normal breech presentation group.

The oxygen saturation of the fetal blood in those three cases did not differ significantly from the mean level at the different sampling periods in the normal breech delivery series. But the umbilical cord blood in Case III showed a marked lowering of the  $\text{SaO}_2$ .

## COMMENTS

The present series of 15 breech delivery cases meets all reasonable claims of normality. All the infants were delivered by the vaginal route with no or only minor obstetrical intervention. The newborn infants were term, mature, and had a one-minute Apgar score of 8-10.

As no systematic studies seem to have appeared previously on fetal blood sampled during labour in the breech presentation, the results of the pre-

sent investigation were in the first place compared with those found in a series of completely normal cases delivered in the vertex presentation. The representativity of fetal scalp blood composition as related to the blood of the main systemic circulation of the fetus is well documented (cf. i. a. Gare et al. 1967; Adamsons et al. 1968; Teramo 1969; Yoshiooka & Roux 1970). In the present study, no statistically significant differences were recorded at different periods in the course of labour between the normal breech delivery series and the control series concerning the parameters investigated; the only exception being a somewhat lower fetal  $BD_{ECF}$  and lactate mean values in the first stage of labour in the breech presentation series. In addition, determinations made in fetal blood at the most terminal phase of labour were in both series equally well related to those made in umbilical cord blood at birth.

Thus it would seem that fetal blood sampled during labour in the breech presentation is, concerning acid-base and related metabolic components, as representative of the blood in the main circulation as is the fetal scalp blood sampled in the vertex presentation. This is interesting in view of the haemodynamic differences between the lower and the upper fetal circulation (the slightly higher mean level of fetal  $Pco_2$  in the breech series is probably an expression for the different circulatory conditions existing in the breech and in the vertex presentation).

The observation made implies as a consequence that the patterns of changes pertaining to the different blood components during the course of labour are principally the same in normal breech and normal vertex deliveries. Thus, for instance, the normally encountered pattern of a moderate metabolic acidification developing in the maternal blood during labour (i. e. increased BD and lactate) was similarly found in both series. At the same time, the mean BD level in fetal blood was, in the breech as well as in the control series, constantly lower than the maternal level ( $\angle BD_{ECF}$  value positive), as is also known to be the case normally. In both series, the maternal glucose metabolism was similarly activated--probably as a stress response--as seen from the rising blood glucose concentration. The glucose increase seen in the fetal blood, equal in both series, is secondary to the maternal increase, as also seen from the fact that the glucose concentration was higher in umbilical vein blood than in umbilical artery blood at birth.

However, despite the overall statistical agreement between the results found in the breech and in the control series, some diverging tendencies could be noted at the end of labour. Fetal pH tended to decrease somewhat more in the breech presentation series at the terminal sampling period of labour. This was correlated with a more marked increase in the fetal  $Pco_2$ . (It should be pointed out in this context that the lines in



the Figures connect mean values and do not express the true course of changes over time. The  $\text{Pco}_2$  increase in Fig. 2, therefore, is more likely to occur close to sampling period 7 than to be of a linear character.) As a consequence of the fetal pH fall, the maternal-fetal pH difference ( $\Delta\text{pH}$ ) was higher in the breech delivery series than in the control series at the terminal phase of labour, the value being around 0.20 pH units, which in the vertex presentation has been considered to be a borderline between normal conditions and imminent fetal hypoxia (cf. Jacobson 1970; Jacobson *et al.* 1971; Khazin & Hon 1971; Heinrich *et al.* 1972; Rooth *et al.* 1972, 1973; Seidenschnur *et al.* 1973).

Those findings should be considered together with the somewhat higher end-value of fetal plasma lactate in the breech series, and also together with the results obtained when repeated samples were drawn at very short intervals at the terminal phase of labour. Technically, this was possible only in some of the breech delivery cases, but it was found then that the fetal  $\text{BD}_{\text{ECF}}$  level was distinctly apt to rise very quickly.

The results of the present study thus indicate that during the main course of labour no significant differences are likely to be found between the normal breech and the normal vertex presentation regarding metabolic components of the fetal blood, reflecting the oxygen supply. However, the results also clearly indicate that the last 10–15 minutes of labour, and in particular the very last minutes before delivery, are in this respect more critical to the fetus presenting by the breech than to the fetus presenting by the vertex. The biochemical observations made in the three cases of fetal depression at birth favour this view. In all three, there was a marked metabolic acidification in the fetal blood sampled immediately before birth and in the umbilical cord blood, although no clinical signs of fetal distress had been recorded before delivery in two of the cases. Similar conclusions have been advanced by Kubli *et al.* (1971); Serreyn *et al.* (1973); and Schwenzel *et al.* (1973) on the basis of umbilical cord blood studies in breech deliveries.

The obstetrical-clinical management of breech presentation should consequently be of such a kind as to facilitate and shorten as much as possible the terminal phase of labour. A routine that includes not only prophylactic episiotomy and release of the arms, but also the immediate use of forceps on the aftercoming head when the simple Bracht manoeuvre does not produce prompt effect, would seem advisable (cf. Hill & Eliot 1973).

The discussion of the results has hitherto been based on the mean values of the different parameters found in the whole series of cases. The variance of individual observations, as evident from the Tables and the Figures, will of course to some extent limit the diagnostic value of single

determinations in separate cases. This problem, similar to that of fetal scalp blood analyses, has been discussed earlier (Jacobson 1970). However, we consider the application of this method in the intensive care of breech presentation cases justified and clinically informative, provided that repeated samples are drawn in the course of labour to reveal quantitative changes of the fetal blood constituents, and provided that the relation between maternal and fetal blood components, particularly the  $\Delta$  pH value, is unexceptionally determined. In view of this, "fetal breech blood" seems to have clinical significance equal to that already established for "fetal scalp blood".

## SUMMARY

Fetal and maternal acid-base and glucose metabolism was studied through the course of labour in a series of 15 obstetrically normal breech delivery cases. The infants were all mature and had a normal Apgar score at birth. The results were compared with those found in a control series of 16 normal cases delivered in vertex presentation. From statistical comparison of the mean levels of the parameters determined at different periods during labour and in umbilical cord blood at birth in the two series, it is concluded that the fetal blood obtained in the breech presentation is as representative of the blood of the fetal main circulation as is the scalp blood.

The overall pattern of changes shown by the different blood components studied favours the view that the most critical phase for the fetus during breech delivery is concentrated to the very last minutes of labour. Measures aimed at shortening this phase as much as possible should therefore be made a routine, as very rapid changes in the sense of raised  $P_{CO_2}$  and increased Base Deficit are apt to occur in the fetal blood at that time. This view was also supported by results obtained in three cases of breech delivery with signs of fetal distress at birth.

The use of fetal blood analysis should, in our opinion, hold the same position in monitoring the intra-partum condition of the fetus in the breech presentation as in the vertex presentation.

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FETAL AND MATERNAL ACID-BASE BALANCE, CARBOHYDRATE  
AND LIPID METABOLISM IN RELATION TO DIFFERENT SIGNS OF  
FETAL DISTRESS DURING LABOUR

Stig Gårdmark, Lennart Jacobson & Gösta Rooth



The currently developed techniques for continuous recording of the fetal heart rate (FHR) and for intermittent biochemical determinations of different fetal scalp blood components during labour have substantially extended the possibilities of evaluating the classical and rather inaccurate signs of fetal distress, i.e. fetal heart rate abnormalities found at auscultation and passage of meconium. However, several uncertainties and divergences of opinion still pertain to the interpretation and clinical application of data obtained by these techniques, basically because a strict and unequivocal definition of fetal distress per se is not yet available either in the fetus or in the newborn infant at birth.

Several authors have reported on the correlation between various abnormal FHR patterns - particularly decelerations - and/or passage of meconium, on the one hand, and changes in fetal scalp blood biochemistry, on the other. The fetal blood determinations in these studies have been mainly referred to pH or to the acid-base balance (Caldeyro-Barcia *et al.* 1968, Coltart *et al.* 1969, Kubli *et al.* 1969, Wood *et al.* 1969, Bowe *et al.* 1970, Grimwade 1970, de la Rama & Merkatz 1970, Beard *et al.* 1971, Hobel 1971, Natrass 1971, Tipton & Shelley 1971, O'Gureck *et al.* 1972), although occasionally plasma lactate and pyruvate have been determined (Schmid & Bretscher 1970). The results are not uniform. Although very pronounced FHR disturbances generally show a fairly high correlation to fetal acid-base changes in the direction of acidosis, the correlation between moderate FHR abnormalities (decelerations as well as accelerations) and fetal biochemical disturbances is less clear. The same would seem to apply to meconium-staining of the amniotic fluid. Only heavy meconium-staining is unambiguously reported to correlate with fetal acidosis (Hobel 1971). It is also open to discussion whether FHR alternations are more sensitive and earlier-appearing indicators of fetal hypoxia than metabolic changes in the fetal blood, or vice versa. It has been claimed, *i.a.* by Wood (1967) and by Simmons & Lieberman (1972), that FHR changes should be expected to precede fetal acid-base disturbances, whereas several reports have appeared on even very low fetal pH values in the absence of any FHR irregularities (see Coltart *et al.* 1969, Berg *et al.* 1970, Cohen *et al.* 1971, Thalme *et al.* 1972).

Standards adopted by different authors to define normal range and limits of fetal acid-base components still rather vary as illustrated for pH in Table I. The different standards present in the literature were subjected to discriminating analysis by Lumley *et al.* (1971) who stated that pH 7.25 should be considered the lower normal limit, and also by Kubli *et al.* (1972) who were more apt to regard pH 7.20 as the lower normal limit. Kubli *et al.*, on the basis of approximately 1,800 determinations, found that about 3% of unselected fetuses had a scalp blood pH < 7.20 in the first stage of labour, the same applying to about 16% at the end of the second stage.

Different subgroups of pre-pathological pH limits have been tentatively proposed; for instance, 7.25-7.20 (Saling 1966, Cohen et al. 1971); 7.20-7.15 (Wood et al. 1969); 7.25-7.24 and 7.23-7.21 (Coltart et al. 1969).

Table I. Lower normal limits of fetal scalp blood pH, adopted by different authors.

|                                          | 1st stage | 2nd stage |
|------------------------------------------|-----------|-----------|
| Saling (1963), Bretscher & Saling (1967) | 7.20      | 7.20      |
| Beard & Morris (1965)                    | 7.20      | 7.17      |
| Paul <u>et al.</u> (1967)                | 7.20      | 7.20      |
| Kubli (1968)                             | 7.21      | 7.23      |
| Berg <u>et al.</u> (1970)                | 7.23      | 7.23      |
| Grimwade (1970)                          | 7.25      | 7.25      |
| Lumley <u>et al.</u> (1970)              | 7.25      | 7.25      |
| Paterson <u>et al.</u> (1970)            | 7.23      | 7.17      |
| Cohen <u>et al.</u> (1971)               | 7.20      | 7.20      |
| Hobel (1971)                             | 7.25      | 7.25      |
| Seidenschnur & Heinrich (1973)           | 7.18      | 7.18      |

Several authors have advocated that the fetal acid-base values are more informative when related to corresponding maternal values. This applies in particular to the maternal-fetal pH difference, the  $\Delta\text{pH}$  value (Jacobson 1970, Khazin & Hon 1971 a & b, Vretos 1971, Rooth et al. 1973, Seidenschnur et al. 1973, Gårdmark et al. 1974 a, b, c, Jacobson et al. 1974). According to our previous studies, a  $\Delta\text{pH}$  between 0.15-0.20 pH units should arouse suspicion of impaired fetal gas exchange and a  $\Delta\text{pH} > 0.20$  pH units can usually be considered abnormal. Other authors (Beard 1968, Vretos 1971) have stressed the importance of estimating the maternal-fetal base deficit difference ( $\Delta\text{BD}$ ) or the  $\Delta\text{BD}$  calculated for the entire extracellular fluid compartment,  $\Delta\text{BD}_{\text{ECF}}$ , (Roversi & Canussio 1970, Seidenschnur & Heinrich 1973).

The specific problems connected with the assessment of fetal hypoxic conditions at birth by means of Apgar scoring are dealt with by i. a. James et al. (1968) and Bowe et al. (1970). Relating the Apgar score to fetal acid-base balance, they pointed to the many factors other than impaired oxygenation that could account for a low Apgar score ('false normals'), maternal sedation being the most prominent of them. This brief survey merely aims at illustrating the numerous difficulties inherent in investigations of fetal distress conditions in man.

The purpose of the present study was twofold: 1) To analyse the metabolic significance of various clinical signs of fetal distress in well-defined

groups of cases by means of determinations of the simultaneous maternal and fetal acid-base balance (pH,  $P_{CO_2}$ ,  $BD_{ECF}$ ), plasma lactate, pyruvate, glucose,  $\beta$ -hydroxybutyrate, and glycerol (occasionally also  $O_2$ -saturation and plasma sodium); 2) To compare the different biochemical variables determined in the different groups in attempting to distinguish the variable(s) that might be considered most informative and feasible for clinical routine practice.

## MATERIAL AND METHODS

The total series comprises 91 parturients, including a control group of 19 normal-delivery patients. The series was divided into separate groups according to the specific clinical signs of fetal distress. The groups, denoted A-F, are briefly presented in Table II and defined in detail below. A primary series of 110 randomly selected patients with signs of fetal distress was investigated in order to select the present subjects that adequately fit the chosen criteria. The investigation covers the period January 1971 through August 1973. All samples were taken by the same person and with the same technique, and the chemical determinations were throughout performed by the same laboratory assistants at special research laboratories.

The FHR abnormalities were usually initially detected by auscultation. From the moment during labour when the subjects were included into the investigation, monitoring of the FHR by means of scalp electrode and a Roche Cardiotocograph V (in combination with intrauterine pressure recording) was usually started. The same applies to the group presenting passage of meconium as the only sign. In order not to influence the department's established obstetrical routine, the results of the blood determinations were not disclosed to the obstetrician-in-charge.

## THE DIFFERENT GROUPS OF CASES

Series A. Meconium-stained amniotic fluid (normal FHR).

The group consists of 20 patients. The meconium-staining was moderate in ten and heavy in ten. The FHR showed no abnormalities throughout labour



Table II. Definition and some background data of the different groups.

| <u>Groups</u>                                                  | <u>n</u> | <u>Primiparae/<br/>multiparae</u> | <u>Mean maternal<br/>age and range</u> | <u>Mean birth-<br/>weight and range</u> | <u>No. of cases with<br/>Apgar score <math>\leq 7</math></u> |
|----------------------------------------------------------------|----------|-----------------------------------|----------------------------------------|-----------------------------------------|--------------------------------------------------------------|
| A) Meconium-stained<br>amniotic fluid                          | 20       | 15/5                              | 24.5 (18-35)                           | 3369 (2650-4260)                        | 2                                                            |
| B) Fetal bradycardia<br>and meconium-stained<br>amniotic fluid | 20       | 20/0                              | 24.8 (18-33)                           | 3307 (1950-4280)                        | 5                                                            |
| C) Fetal bradycardia                                           | 16       | 11/5                              | 25.4 (17-32)                           | 3296 (2100-4380)                        | 2                                                            |
| D) Fetal tachycardia                                           | 12       | 9/3                               | 24.4 (19-29)                           | 3783 (2530-4760)                        | 2                                                            |
| E) Low one-minute<br>Apgar score                               | 14       | 11/3                              | 24.8 (17-32)                           | 3516 (1950-4400)                        | 14                                                           |
| F) Normal controls                                             | 19       | 18/1                              | 24.4 (17-34)                           | 3419 (2700-4200)                        | 0                                                            |

in any of them. In 18 of the patients, simultaneous maternal and fetal samples were drawn in the first stage of labour after diagnosing the passage of meconium. A second sample was taken from five of them in the second stage of labour because of increased meconium-staining. In the remaining two, passage of meconium appeared in the second stage of labour and occasioned sampling at that stage only.

In four of the 20, labour was terminated by vacuum-extraction, the others being spontaneously delivered. Five fetuses had tight cord-around-the-neck. Two were moderately depressed at birth, the one-minute Apgar score being 5 and 7, respectively. All had a five-minute Apgar score of 8-10.

#### Series B. Meconium-stained amniotic fluid and fetal bradycardia.

The group comprises 20 parturients. Sampling was performed in situations of base-line fetal bradycardia ( $FHR < 120$  bpm), persistent during two or more uterine contraction cycles, or of repeated variable and late decelerations, and meconium-stained liquor. In 18 patients, simultaneous maternal and fetal samples were taken in ten cases during the first stage of labour, and in ten during the second stage. In two, only maternal samples immediately before delivery and umbilical cord blood samples were taken.

Labour was terminated by caesarean section in three, by vacuum-extraction in six, and by low forceps in two. Five fetuses of the series had tight cord-around-the-neck, and in another two, umbilical cord prolapse occurred. Five infants (three of them being spontaneously delivered) were depressed at birth, the one-minute Apgar score being 5, 5, 6, 6, and 7, respectively. After resuscitation, they all showed a five-minute score of 8-10.

#### Series C. Fetal bradycardia (non-stained amniotic fluid).

The series consists of 16 parturients. The indication for blood sampling was base-line fetal bradycardia ( $< 120$  bpm) during at least 10 minutes or at repeated intervals, and repeated variable and late decelerations. Simultaneous maternal and fetal blood samples were drawn in six during the first stage of labour, and in ten in the second stage.

Labour was terminated by low forceps in five and by vacuum-extraction in five. Six fetuses had the cord tightly around the neck. Two infants (both spontaneously delivered) had a one-minute Apgar score of 4 and 6, respectively. After resuscitation, one of them had a five-minute score of 7, and the other a score of 9.

#### Series D. Fetal tachycardia.

The series comprises 12 cases. At sampling, the FHR exceeded 160 bpm during repeated periods with short intervals or had been persistent for more than 20 minutes. Twelve simultaneous samples were drawn in the first stage of labour, and three in the second stage. The latter three samples were subjected to acid-base determinations only.

Labour was terminated by caesarean section in two patients, and by vacuum-extraction in five. One fetus had a tight cord-around-the-neck. Two infants showed a low one-minute Apgar score (3 and 6 points), the five-minute score being 9 in both infants after simple resuscitation procedures.

#### Series E. Low one-minute Apgar score.

The group comprises 14 parturients, whose infants showed a one-minute Apgar score of 7 or less after vaginal delivery. Ten of them were obtained from Groups A-D (one infant with a score of 3 in Group D was excluded in this context, the depression appearing after caesarean section). The remaining four were acquired from the larger primary series. Thirteen simultaneous maternal and fetal blood samples were taken in the first stage of labour and eight in the second stage, the latter all drawn within the final 15 minutes of labour. Umbilical cord blood samples were obtained in 13 of the cases.

Labour was terminated by vacuum-extraction in four and by low forceps in two. Eight fetuses had the cord tightly around the neck. The one-minute Apgar score was 4 in one, 5 in five, 6 in four, and 7 in four. The five-minute score was 8-10 in all except one, which had a score of 7.

#### Series F. Normal controls.

This group comprises 19 parturients with entirely normal pregnancy and labour. All were spontaneously delivered, the infants having a one-minute Apgar score of 8-10. The cases were derived from other normal series

investigated for different purposes during the same time as the present study. The blood sampling and the chemical determinations thus were identically performed in this group and in Groups A-E. As Table II shows, the control group agreed well with Groups A-E concerning the distribution of parity, maternal age, and infant birth-weight. Data were available from 17 simultaneous maternal and fetal samples in the first stage of labour and from 18 samples in the second stage. Sampling of the cord blood at birth was made in 17 of the cases.

## BLOOD SAMPLING AND ASSAY METHODS

As mentioned above, blood sampling in Groups A-D was related to the time when the specific clinical sign or pattern of signs occurred or was detected. In some of the cases, repeated samples were then drawn within a short interval, but in the subsequent analysis and discussion, only one sample was used, selected at random. Thus, all data presented for the first and second stage of labour refer to only one sampling in each case.

Fetal scalp blood was sampled into long, heparinized glass capillaries. Arterialized maternal capillary blood from the finger tip was collected anaerobically into short glass capillary tubes for the immediate acid-base determinations, and aerobically into small plastic tubes adapted for a Beckman high speed microcentrifuge for the plasma determinations of glucose, lactate, pyruvate,  $\beta$ -hydroxybutyrate, glycerol, and sodium. Arterial and venous blood from the clamped umbilical cord at birth was anaerobically drawn into heparinized all-glass syringes.

pH was measured by means of the Radiometer microelectrode unit E 5021 and PHM 27.

$P_{CO_2}$  was determined with the Eschweiler micro- $CO_2$ -electrode assembly. Base deficit was calculated for the entire extracellular fluid compartment ( $BD_{ECF}$ ) from the Siggaard-Andersen alignment nomogram, read at the Hb 5g/100 ml-line (Siggaard-Andersen 1963).

Oxygen saturation ( $SaO_2$ ) was determined photometrically with the micro method devised by Siggaard-Andersen, Jørgensen & Naeraa (1962).

Plasma glucose was determined by means of the glucose oxidase method described by Marks (1959).

Plasma lactate was measured with the ultramicroadapted and slightly modified Boehringer enzymatic-spectrophotometric method (Boehringer Bulletin TC-B 972; Rooth 1967).

Plasma pyruvate was determined fluorometrically by an ultramicro-adaptation of the Boehringer enzymatic method, a spectrofluorometer being used for the final stage (Boehringer Bulletin TC-B 972; Rooth 1967).  $\beta$ -hydroxybutyrate in plasma was measured by means of the  $\beta$ -hydroxybutyrate dehydrogenase method of Williamson *et al.* (1962), modified according to Persson (1970).

Plasma glycerol was determined by the enzymatic fluorometric micro-method described by Laurell and Tibbling (1966).

Sodium in plasma was measured according to the method of Kaplan and del Carmen (1956).

## STATISTICAL METHODS

Paired observation test was used at the analysis of differences within the series. Student's t-test was used for comparison of means between different series. In case of  $\sigma_1$  and  $\sigma_2$  being considered not equal, the Aspin-Welch test was used. Fischer's one-tailed Exact Probability Test was used for comparison between case series and control series when studying a variable dichotomized into two groups.

## RESULTS

pH (Tables III-VIII, Fig. 1). A comparison of Groups A-E, representing the different signs of fetal distress, and the control group (F) revealed that in the first stage of labour the mean maternal pH values in the former groups all exceeded the mean value of 7.45 in the controls. The differences were statistically non-significant except for that between Group C, comprising cases with fetal bradycardia, and the normal group ( $p < 0.01$ ). In the second stage of labour, the maternal pH mean levels in all the groups were slightly lower than in the first stage. The difference of means between the groups was still statistically significant only between Group C and the control group ( $p < 0.01$ ).

In the first stage of labour, the fetal pH mean values of Group A, i.e. those with meconium-stained amniotic fluid, and of the control group were almost identical (7.37 and 7.36, respectively). In the remaining series, the mean fetal pH was lower, the lowest value of 7.32, found in



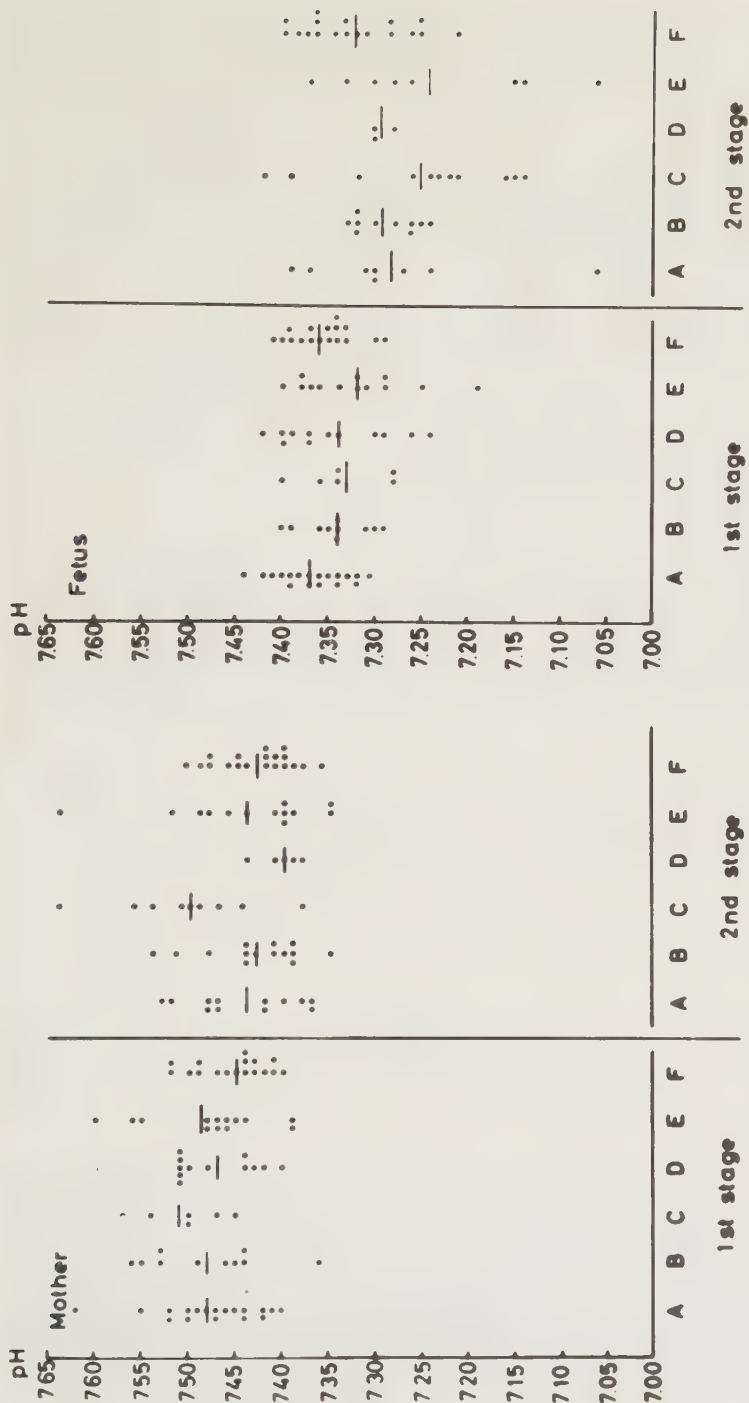


Fig 1. Distribution of maternal and fetal blood pH values, determined in the first and second stage of labour, within the different groups (for definition of the groups, see Table II). Short lines denote the means.

Group E (low Apgar score), differing significantly from the control group ( $p < 0.01$ ). Similar to the findings concerning the maternal pH, the fetal pH means in all groups were lower in the second stage than in the first. It was also found that, in the second stage, the fetal pH mean level of all Groups A-E fell below that of the control group. The lowest pH means were encountered in group C (fetal bradycardia) and in Group E (low Apgar score), being 7.25 and 7.24, respectively. Both these values differed significantly from the pH mean of the control series ( $p < 0.05$ ).

The pH mean levels found in umbilical arterial blood agreed well with the corresponding means found in fetal scalp blood in the second stage of labour, this being valid for all the groups. The highest means were present in the control series and in Group D (fetal tachycardia), both being 7.27. The lowest means appeared in Groups C and E (7.18 and 7.17). The latter values differed significantly from the pH mean of the control group ( $p < 0.05$  and  $p < 0.01$ , respectively).

When the distribution of the individual pH values in umbilical arterial blood within different pH range limits (Table IX) was subjected to statistical analysis, it was found that in Groups B and C taken together, i.e. where there was fetal bradycardia with or without passage of meconium, and also in Group E (low Apgar score), the frequency of pH values below 7.20 was significantly higher than in the control group ( $p < 0.01$ ).

Table IX. Distribution of the umbilical artery blood pH values within certain range limits in the different groups.

| Group        | pH in umbilical artery blood |           |          |
|--------------|------------------------------|-----------|----------|
|              | $\geq 7.20$                  | 7.19-7.15 | $< 7.15$ |
| A            | 8                            | 3         | 1        |
| B            | 11                           | 3         | 1        |
| C            | 8                            | 0         | 6        |
| D            | 5                            | 0         | 1        |
| E            | 8                            | 1         | 4        |
| F (controls) | 17                           | 0         | 0        |

$\Delta$ pH, maternal-fetal pH difference (Fig. 2). Fig. 2 plots the single  $\Delta$ pH values found in the different groups in the first and second stage of labour. The figure shows the frequency distribution of  $\Delta$ pH values below 0.15, between 0.15-0.19, and equal to or more than 0.20 pH units. In the first stage of labour,  $\Delta$ pH values  $\leq 0.20$  were present in three of six cases in Group C, and in four of 13 in Group E. In the second stage,  $\Delta$ pH values  $\leq 0.20$  pH units were related to Groups B, C, and E, the

high  $\Delta\text{pH}$  of these groups usually considerably exceeding the 0.20 limit. Statistically, the frequency of  $\Delta\text{pH}$  values  $\geq 0.20$  was significantly higher in Group E and C than in the control group in the second stage of labour ( $p < 0.05$ ).

The choice of  $\Delta\text{pH} < 0.15$  pH units as a normal standard showed that the frequency of raised  $\Delta\text{pH}$  values was statistically higher in Groups B and C taken together than in the control series ( $p < 0.05$ ), this applied to both first and second stage of labour. In the second stage, Group C alone differed significantly from the control group ( $p < 0.01$ ) in this respect.

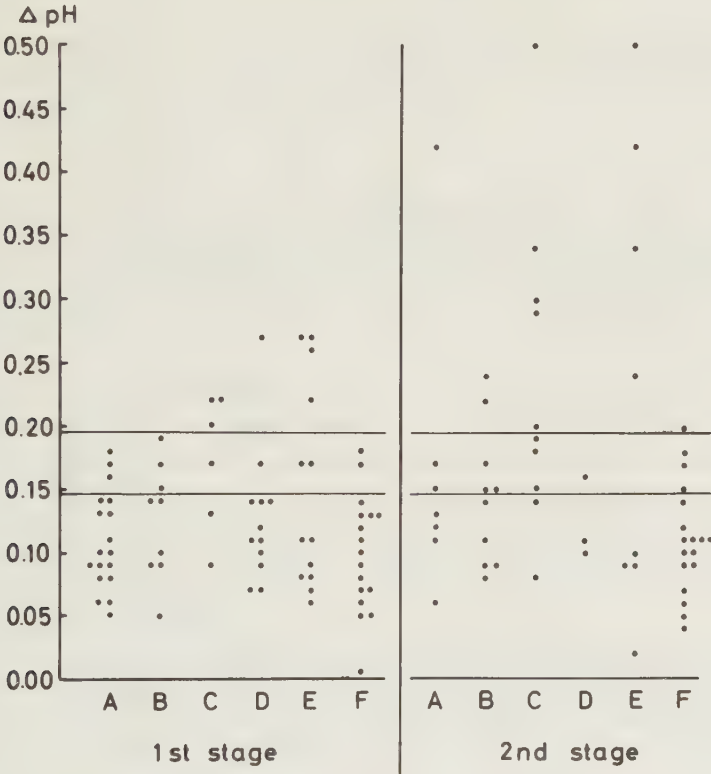


Fig 2. Distribution of  $\Delta\text{pH}$  values, determined in the first and second stage of labour, within the different groups.

$\text{Pco}_2$  (Tables III-VIII, Fig. 3). The maternal  $\text{Pco}_2$  means differed only slightly between the groups, and also between the first and second stage of labour, the mean values being in the range 23-27 mm Hg. Statistically,

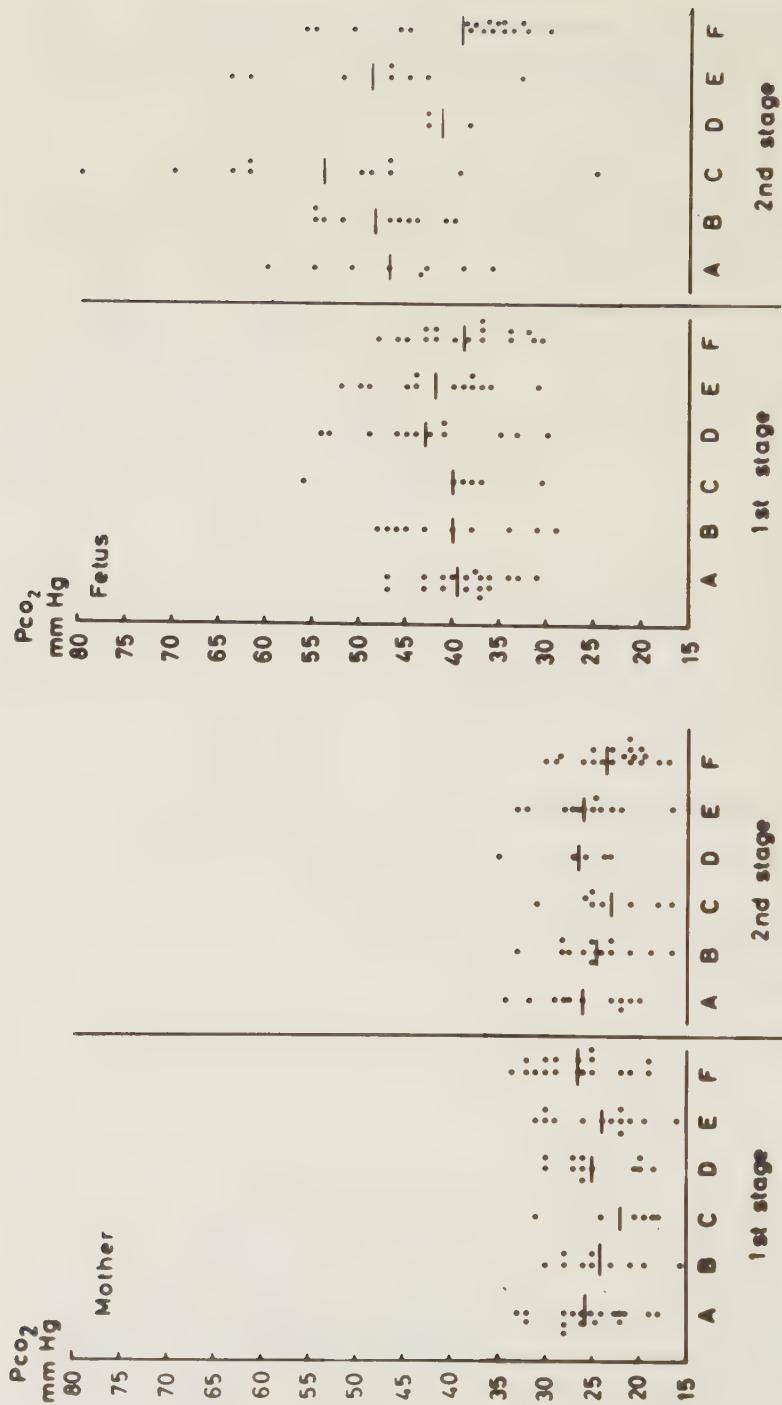


Fig 3. Distribution of maternal and fetal blood PCO<sub>2</sub> values, determined in the first and second stage of labour, within the different groups. Short lines denote the means.

a significant difference was found only between the mean  $P_{CO_2}$  value of Group C (fetal bradycardia) and that of the control group in the first stage of labour, the  $P_{CO_2}$  being lower in the former group ( $p < 0.05$ ).

The fetal  $P_{CO_2}$  mean values were around 40 mm Hg in all the groups in the first stage of labour. In the second stage, the  $P_{CO_2}$  mean levels were higher in all groups except the control series. The highest value in this stage was found in Group C (54.1 mm Hg), differing significantly from the control group ( $p < 0.01$ ). Significant differences were also found between the mean value of the control series and those of Groups A ( $p < 0.05$ ), B ( $p < 0.01$ ), and E ( $p < 0.05$ ).

The  $P_{CO_2}$  mean values obtained for umbilical artery blood in Groups A, B, C, and E were higher than those present in the control group, but the differences were not statistically significant.

$BD_{ECF}$  (Tables III-VIII, Fig. 4) The maternal  $BD_{ECF}$  mean values fell within the range of 4.5-5.6 mmol/l in the entire material in the first stage of labour. In the second stage, the mean levels were throughout somewhat higher (5.8-8.6 mmol/l). No statistically significant differences existed between the groups.

The fetal  $BD_{ECF}$  mean values were lower than the corresponding maternal means in all the groups in the first and also in the second stage of labour. In the first stage, the mean values ranged from 2.3-4.4 mmol/l, and in the second stage, from 3.4-6.0 mmol/l. No statistically significant differences were present between the groups. It was noticeable that the individual  $BD_{ECF}$  values in all the groups were widely scattered. Single values exceeding 10 mmol/l were seen in groups A, B, D, and E, and also in the control group.

The highest  $BD_{ECF}$  mean values in umbilical arterial blood were found in Groups C and E (8.5 and 8.2 mmol/l), and the lowest mean, 5.6 mmol/l, in the control series. The differences were not statistically significant.

$\Delta BD_{ECF}$ , maternal-fetal  $BD_{ECF}$  difference (Fig. 5). As Fig. 5 shows, the single  $\Delta BD_{ECF}$  values had a considerable range of variation in all the groups in both first and second stage of labour. Statistically, no significant differences were present between the groups. The majority of  $\Delta BD_{ECF}$  values were positive, but some negative values (i.e. the fetal  $BD_{ECF}$  exceeding the maternal value) were found in all the groups.



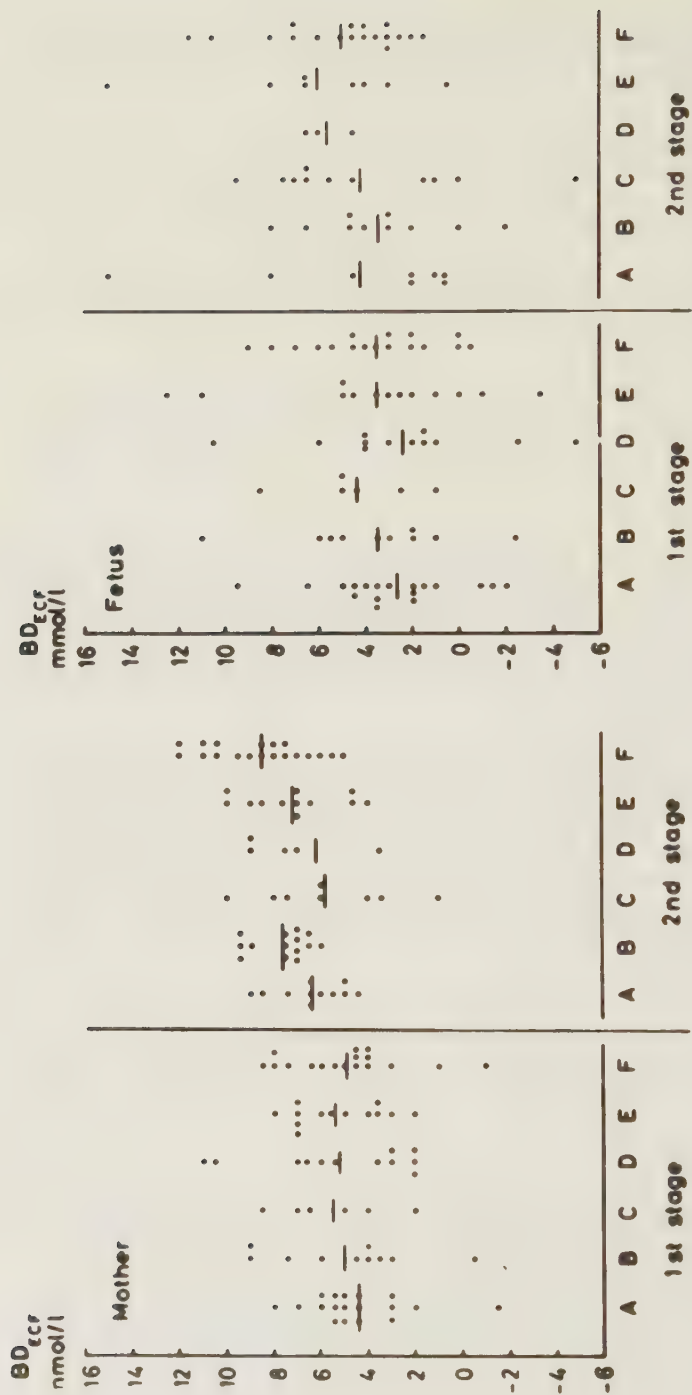


Fig 4. Distribution of maternal and fetal blood  $BD_{ECF}$  blood values, determined in the first and second stage of labour, within the different groups. Short lines denote the means.

The frequency of negative  $\Delta BD_{ECF}$  values did not differ significantly between the groups.

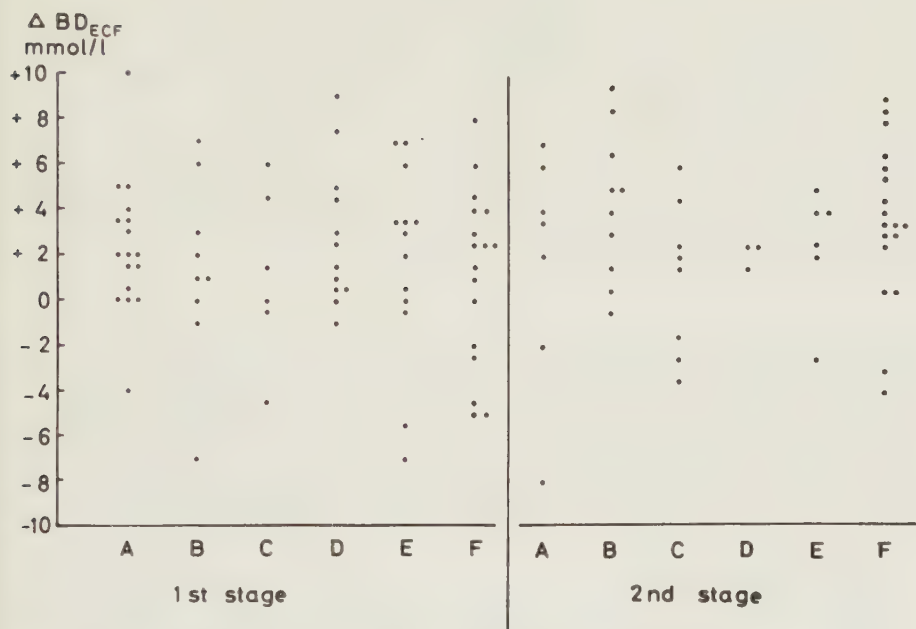


Fig 5. Distribution of  $\Delta BD_{ECF}$  values, determined in the first and second stage of labour, within the different groups.

Oxygen saturation ( $SaO_2$ ) in fetal blood (Tables III-VII). The  $SaO_2$  mean values found in the first stage of labour differed only slightly and non-significantly between Groups A-E ( $SaO_2$  was not determined in the control series). The highest value (58 %sat.) was seen in Group D (fetal tachycardia), and the lowest (49 %sat.) in Group C (fetal bradycardia).

In the second stage of labour, the  $SaO_2$  mean values were approximately 40 %sat. in Groups A, B, and C (no determinations were made in Group D), and 30 %sat. in Group E (low Apgar score).

In the umbilical artery blood, the mean values were within the range of 45-49 %sat. in Groups A-D, and 34 %sat. in Group E. Statistically, the lower mean value in Group E did not differ significantly from the values found in the remaining groups.

Plasma glucose (Tables III-VIII). The maternal mean plasma glucose concentration in the first stage of labour was found to be higher in Groups A-E than in the control group, the mean concentration in the latter being 88 mg%. The differences between the mean value of the controls and those of Groups B, C, and E were statistically significant ( $p < 0.05$ ). In the second stage of labour, the glucose mean values in all groups (no measurements in Group D) were somewhat higher than those found in the first stage and ranged between 109-119 mg%. No statistically significant differences existed between the groups in the second stage.

The fetal mean values of plasma glucose were throughout approximately 20-35 mg% lower than the corresponding maternal ones. No statistically significant differences were present between the mean values of the different groups, including that of the control series.

Plasma lactate (Tables III-VIII, Fig. 6). In the first stage of labour, the maternal plasma lactate mean concentration in all groups was almost identical, the values falling within the range of 2.4-2.9 mmol/l. In the second stage, the mean values ranged from 5.2-6.8 mmol/l, no significant differences between the groups being present. The highest mean value of 6.8 mmol/l applied to Group C (fetal bradycardia). As Fig. 6 shows, the single values covered a rather wide range in every group in the second stage of labour.

The fetal lactate mean values found in the first stage of labour were somewhat higher than the corresponding maternal values in Groups B, C, D, and E. The range of the means, considering all the groups lay between 2.9 and 4.4 mmol/l, the highest value being in Group C. However, this mean value did not differ significantly from that of the control group. The fetal lactate mean concentration in the second stage of labour ranged between 4.3 mmol/l in the control group and 8.8 mmol/l in Group E (low Apgar score). The difference between these two means was statistically significant ( $p < 0.01$ ), as was the difference between the mean value in Group C (6.6 mmol/l) and that of the controls ( $p < 0.01$ ).

In the umbilical artery blood, the mean concentration of plasma lactate in Groups C and E (8.4 and 8.2 mmol/l, respectively) also differed significantly from the mean of the control group, 5.4 mmol/l ( $p < 0.05$ ).

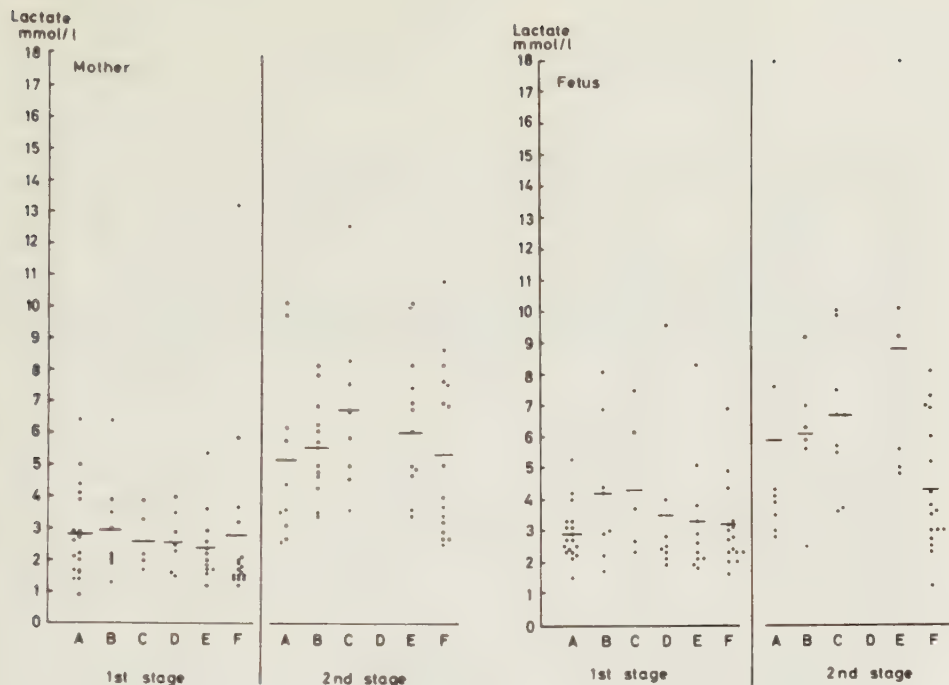


Fig 6. Distribution of maternal and fetal plasma lactate values, determined in the first and second stage of labour, within the different groups. Short lines denote the means.

Plasma pyruvate (Tables III-VIII). The mean values of the maternal plasma pyruvate were within the range of 0.12-0.16 mmol/l in the first stage of labour, and within the range of 0.20-0.26 mmol/l in the second stage. No statistically significant differences were found between the groups in the first and second stage. The highest mean values applied to the control group.

The mean fetal plasma pyruvate concentration of the different groups ranged from 0.10-0.13 mmol/l in the first stage of labour, and from 0.15-0.19 mmol/l in the second stage. No significant differences were present between the groups.

The highest mean value of the umbilical artery blood, 0.21 mmol/l, was found in the control group, the mean values of the remaining groups ranging from 0.13-0.18 mmol/l.

Table III. Different maternal (M) and fetal (F) blood components, determined in the first and second stage of labour and in umbilical cord blood in series A (meconium-stained amniotic fluid and normal FHR).  
Mean values, standard deviations, and 95% confidence limits of the means.

|                              | 1st stage |                                     |                    | 2nd stage |                                     |                    | Umbilical vessels |                                     |                    |      |
|------------------------------|-----------|-------------------------------------|--------------------|-----------|-------------------------------------|--------------------|-------------------|-------------------------------------|--------------------|------|
|                              | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 | n                 | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 |      |
| pH                           | M         | 18                                  | 7.48<br>$\pm 0.03$ | 0.06      | 11                                  | 7.44<br>$\pm 0.04$ | 0.05              | Vein 12                             | 7.32<br>$\pm 0.06$ | 0.09 |
|                              | F         | 18                                  | 7.37<br>$\pm 0.02$ | 0.04      | 8                                   | 7.28<br>$\pm 0.08$ | 0.10              | Artery 12                           | 7.23<br>$\pm 0.06$ | 0.10 |
| Pco <sub>2</sub><br>mm Hg    | M         | 18                                  | 25.5<br>$\pm 2.1$  | 4.3       | 11                                  | 26.0<br>$\pm 3.2$  | 4.7               | V 12                                | 38.3<br>$\pm 4.6$  | 7.3  |
|                              | F         | 18                                  | 38.7<br>$\pm 2.2$  | 4.4       | 8                                   | 46.8<br>$\pm 6.8$  | 8.1               | A 12                                | 48.3<br>$\pm 6.4$  | 10.1 |
| BD <sub>ECF</sub><br>mmol/l  | M         | 18                                  | 4.5<br>$\pm 1.1$   | 2.1       | 11                                  | 6.4<br>$\pm 0.9$   | 1.5               | V 12                                | 5.7<br>$\pm 2.0$   | 3.1  |
|                              | F         | 18                                  | 2.9<br>$\pm 1.4$   | 2.9       | 8                                   | 4.2<br>$\pm 4.2$   | 5.1               | A 12                                | 6.5<br>$\pm 2.2$   | 3.3  |
| SaO <sub>2</sub><br>per cent | F         | 12                                  | 53<br>$\pm 8$      | 12.0      | 6                                   | 41<br>$\pm 16$     | 16                | V 8                                 | 73<br>$\pm 13$     | 15   |
|                              |           |                                     |                    |           |                                     |                    |                   | A 8                                 | 48<br>$\pm 17$     | 21   |



|                    |   |    |                 |       |    |                 |       |   |    |                 |       |
|--------------------|---|----|-----------------|-------|----|-----------------|-------|---|----|-----------------|-------|
| Glucose<br>mg%     | M | 18 | 96<br>±7        | 14    | 10 | 109<br>±19      | 27    | V | 12 | 83<br>±12       | 19    |
|                    | F | 18 | 71<br>±7        | 13    | 8  | 82<br>±18       | 21    | A | 12 | 64<br>±11       | 17    |
| Lactate<br>mmol/l  | M | 18 | 2.8<br>±0.7     | 1.5   | 10 | 5.2<br>±2.0     | 2.8   | V | 12 | 5.3<br>±2.1     | 3.4   |
|                    | F | 18 | 2.9<br>±0.4     | 0.9   | 8  | 5.9<br>±4.2     | 5.1   | A | 12 | 5.9<br>±2.4     | 3.7   |
| Pyruvate<br>mmol/l | M | 17 | 0.13<br>±0.03   | 0.06  | 10 | 0.20<br>±0.04   | 0.05  | V | 12 | 0.15<br>±0.04   | 0.07  |
|                    | F | 17 | 0.11<br>±0.02   | 0.04  | 8  | 0.17<br>±0.05   | 0.06  | A | 12 | 0.14<br>±0.03   | 0.05  |
| β-HB-<br>mmol/l    | M | 18 | 0.96<br>±0.36   | 0.72  | 10 | 1.17<br>±0.47   | 0.66  | V | 12 | 0.62<br>±0.26   | 0.40  |
|                    | F | 18 | 0.25<br>±0.08   | 0.19  | 8  | 0.45<br>±0.20   | 0.26  | A | 12 | 0.44<br>±0.20   | 0.32  |
| Glycerol<br>mmol/l | M | 18 | 0.170<br>±0.036 | 0.072 | 10 | 0.225<br>±0.066 | 0.092 | V | 12 | 0.098<br>±0.037 | 0.060 |
|                    | F | 18 | 0.054<br>±0.015 | 0.031 | 8  | 0.078<br>±0.052 | 0.062 | A | 12 | 0.070<br>±0.027 | 0.043 |
| Sodium<br>mmol/l   | M | 16 | 138.9<br>±3.6   | 6.8   | 9  | 141.6<br>±6.4   | 8.4   | V | 12 | 142.9<br>±5.3   | 8.2   |
|                    | F | 18 | 139.8<br>±3.4   | 7.0   | 8  | 145.3<br>±7.3   | 8.9   | A | 12 | 148.3<br>±9.7   | 15.4  |

Table IV. Different maternal (M) and fetal (F) blood components, determined in the first and second stage of labour and in umbilical cord blood in series B (meconium-stained amniotic fluid and fetal bradycardia).  
Mean values, standard deviations, and 95 % confidence limits of the means.

|                              | 1st stage |                                     |                | 2nd stage |                                     |                | Umbilical vessels |                                     |                |    |
|------------------------------|-----------|-------------------------------------|----------------|-----------|-------------------------------------|----------------|-------------------|-------------------------------------|----------------|----|
|                              | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd             | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd             | n                 | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd             |    |
| pH                           | M 10      | 7.48<br>$\pm 0.05$                  | 0.06           | 14        | 7.43<br>$\pm 0.03$                  | 0.05           | Vein 15           | 7.31<br>$\pm 0.04$                  | 0.08           |    |
|                              | F 10      | 7.34<br>$\pm 0.02$                  | 0.04           | 10        | 7.29<br>$\pm 0.02$                  | 0.03           | Artery 15         | 7.24<br>$\pm 0.03$                  | 0.06           |    |
| Pco <sub>2</sub><br>mm Hg    | M 10      | 24.2<br>$\pm 3.0$                   | 4.2            | 14        | 24.5<br>$\pm 2.4$                   | 4.2            | V 15              | 44.0<br>$\pm 7.0$                   | 12.6           |    |
|                              | F 10      | 40.1<br>$\pm 4.9$                   | 6.9            | 10        | 47.9<br>$\pm 4.1$                   | 5.7            | A 15              | 49.3<br>$\pm 7.4$                   | 13.4           |    |
| BD <sub>ECF</sub><br>mmol/l  | M 10      | 5.0<br>$\pm 2.0$                    | 2.9            | 14        | 7.6<br>$\pm 0.7$                    | 1.2            | V 15              | 4.4<br>$\pm 2.5$                    | 4.4            |    |
|                              | F 10      | 3.7<br>$\pm 2.5$                    | 3.6            | 10        | 3.4<br>$\pm 2.1$                    | 2.9            | A 15              | 5.7<br>$\pm 2.4$                    | 4.3            |    |
| SaO <sub>2</sub><br>per cent | F         | 8                                   | 54<br>$\pm 11$ | 13        | 7                                   | 46<br>$\pm 13$ | 15                | V 11                                | 57<br>$\pm 15$ | 22 |
|                              |           |                                     |                |           |                                     |                |                   | A 11                                | 45<br>$\pm 13$ | 20 |

|                       |   |   |                 |       |    |                 |       |   |    |                 |       |
|-----------------------|---|---|-----------------|-------|----|-----------------|-------|---|----|-----------------|-------|
| Glucose<br>mg%        | M | 9 | 110<br>±22      | 28    | 13 | 113<br>±12      | 20    | V | 15 | 85<br>±11       | 19    |
|                       | F | 8 | 74<br>±21       | 25    | 6  | 87<br>±18       | 17    | A | 15 | 73<br>±12       | 22    |
| Lactate<br>mmol/l     | M | 9 | 2.9<br>±1.2     | 1.6   | 13 | 5.6<br>±0.9     | 1.5   | V | 15 | 6.7<br>±1.4     | 2.5   |
|                       | F | 8 | 4.2<br>±1.9     | 2.3   | 6  | 6.1<br>±2.3     | 2.2   | A | 14 | 6.8<br>±1.6     | 2.8   |
| Pyruvate<br>mmol/l    | M | 9 | 0.13<br>±0.07   | 0.09  | 12 | 0.22<br>±0.08   | 0.12  | V | 15 | 0.19<br>±0.07   | 0.13  |
|                       | F | 7 | 0.13<br>±0.04   | 0.05  | 6  | 0.18<br>±0.10   | 0.09  | A | 15 | 0.18<br>±0.06   | 0.10  |
| $\beta$ -HB<br>mmol/l | M | 9 | 0.72<br>±0.35   | 0.46  | 13 | 1.33<br>±0.45   | 0.74  | V | 15 | 0.58<br>±0.19   | 0.34  |
|                       | F | 8 | 0.21<br>±0.10   | 0.12  | 6  | 0.56<br>±0.36   | 0.32  | A | 15 | 0.48<br>±0.08   | 0.29  |
| Glycerol<br>mmol/l    | M | 8 | 0.122<br>±0.032 | 0.038 | 13 | 0.175<br>±0.026 | 0.043 | V | 15 | 0.064<br>±0.015 | 0.027 |
|                       | F | 8 | 0.059<br>±0.016 | 0.046 | 6  | 0.063<br>±0.024 | 0.021 | A | 15 | 0.055<br>±0.015 | 0.027 |
| Sodium<br>mmol/l      | M | 7 | 139.9<br>±4.4   | 4.7   | 10 | 137.8<br>±5.2   | 7.1   | V | 11 | 142.5<br>±4.4   | 6.5   |
|                       | F | 7 | 137.7<br>±3.0   | 3.2   | 4  | 137.0<br>±3.2   | 5.5   | A | 11 | 148.6<br>±6.2   | 9.2   |

Table V. Different maternal (M) and fetal (F) blood components, determined in the first and second stage of labour and in umbilical cord blood in series C (non-stained amniotic fluid and fetal bradycardia).  
Mean values, standard deviations, and 95 % confidence limits of the means.

|                              | 1st stage |                                     |                    | 2nd stage |                                     |                    | Umbilical vessels |                                     |                    |                |    |
|------------------------------|-----------|-------------------------------------|--------------------|-----------|-------------------------------------|--------------------|-------------------|-------------------------------------|--------------------|----------------|----|
|                              | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 | n                 | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 |                |    |
| pH                           | M         | 6                                   | 7.51<br>$\pm 0.05$ | 0.04      | 9                                   | 7.50<br>$\pm 0.06$ | 0.07              | Vein 14                             | 7.31<br>$\pm 0.05$ | 0.09           |    |
|                              | F         | 6                                   | 7.33<br>$\pm 0.05$ | 0.05      | 11                                  | 7.25<br>$\pm 0.06$ | 0.09              | Artery 14                           | 7.18<br>$\pm 0.08$ | 0.15           |    |
| Pco <sub>2</sub><br>mm Hg    | M         | 6                                   | 21.9<br>$\pm 5.1$  | 4.9       | 8                                   | 23.3<br>$\pm 3.9$  | 4.6               | V                                   | 38.2<br>$\pm 4.7$  | 8.1            |    |
|                              | F         | 6                                   | 40.2<br>$\pm 8.7$  | 8.4       | 11                                  | 54.1<br>$\pm 10.3$ | 15.3              | A                                   | 51.4<br>$\pm 8.6$  | 15.0           |    |
| BDEF<br>mmol/l               | M         | 6                                   | 5.6<br>$\pm 2.6$   | 2.5       | 8                                   | 5.8<br>$\pm 2.4$   | 2.9               | V                                   | 6.3<br>$\pm 2.2$   | 3.7            |    |
|                              | F         | 6                                   | 4.4<br>$\pm 2.7$   | 2.6       | 11                                  | 4.1<br>$\pm 2.8$   | 4.2               | A                                   | 8.5<br>$\pm 3.8$   | 6.5            |    |
| SaO <sub>2</sub><br>per cent | F         | 4                                   | 49<br>$\pm 32$     | 23        | 6                                   | 41<br>$\pm 29$     | 25                | V                                   | 8                  | 79<br>$\pm 13$ | 16 |
|                              |           |                                     |                    |           |                                     |                    |                   | A                                   | 9                  | 49<br>$\pm 12$ | 15 |

|                       |   |   |                           |       |   |                           |       |   |    |                           |       |
|-----------------------|---|---|---------------------------|-------|---|---------------------------|-------|---|----|---------------------------|-------|
| Glucose<br>mg%        | M | 5 | 102<br>+15<br>-10         | 12    | 9 | 114<br>+19<br>-14         | 25    | V | 14 | 85<br>+6<br>-11           | 10    |
|                       | F | 5 | 72<br>+10                 | 8     | 9 | 74<br>+14                 | 18    | A | 13 | 62<br>+11                 | 19    |
| Lactate<br>mmol/l     | M | 5 | 2.6<br>+1.1<br>-2.8       | 0.9   | 8 | 6.8<br>+2.3<br>-1.8       | 2.8   | V | 14 | 7.0<br>+1.4<br>-2.3       | 2.4   |
|                       | F | 5 | 4.4<br>+2.8               | 2.3   | 9 | 6.6<br>+1.8               | 2.3   | A | 14 | 8.4<br>+2.3               | 4.0   |
| Pyruvate<br>mmol/l    | M | 4 | 0.13<br>+0.05<br>-0.03    | 0.03  | 9 | 0.20<br>+0.04<br>-0.03    | 0.06  | V | 14 | 0.14<br>+0.02<br>-0.02    | 0.04  |
|                       | F | 5 | 0.13<br>+0.03             | 0.02  | 8 | 0.15<br>+0.03             | 0.04  | A | 13 | 0.15<br>+0.02             | 0.03  |
| $\beta$ -HB<br>mmol/l | M | 3 | 0.82<br>+0.75<br>-0.27    | 0.41  | 6 | 0.84<br>+0.33<br>-0.16    | 0.32  | V | 10 | 0.50<br>+0.22<br>-0.13    | 0.31  |
|                       | F | 4 | 0.32<br>+0.27             | 0.20  | 6 | 0.32<br>+0.16             | 0.15  | A | 10 | 0.33<br>+0.13             | 0.19  |
| Glycerol<br>mmol/l    | M | 5 | 0.160<br>+0.070<br>-0.025 | 0.056 | 9 | 0.242<br>+0.051<br>-0.022 | 0.066 | V | 14 | 0.087<br>+0.015<br>-0.013 | 0.025 |
|                       | F | 4 | 0.052<br>+0.025           | 0.016 | 6 | 0.078<br>+0.022           | 0.021 | A | 13 | 0.068<br>+0.013           | 0.021 |
| Sodium<br>mmol/l      | M | 4 | 136.5<br>+7.6<br>-4.8     | 4.8   | 6 | 137.8<br>+4.4<br>-3.7     | 4.1   | V | 11 | 145.3<br>+8.5<br>-7.9     | 12.4  |
|                       | F | 4 | 139.0<br>+4.8             | 2.9   | 7 | 136.0<br>+3.7             | 3.9   | A | 10 | 145.7<br>+7.9             | 10.9  |



Table VI. Different maternal (M) and fetal (F) blood components, determined in the first and second stage of labour and in umbilical cord blood in series D (series of tachycardia).  
Mean values, standard deviations, and 95 % confidence limits of the means.

|                              | 1st stage |                                     |                    | 2nd stage |                                     |                    | Umbilical vessels |                                     |    |                    |      |
|------------------------------|-----------|-------------------------------------|--------------------|-----------|-------------------------------------|--------------------|-------------------|-------------------------------------|----|--------------------|------|
|                              | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd<br>conf lim     | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd<br>conf lim     | n                 | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd |                    |      |
| pH                           | M         | 12                                  | 7.47<br>$\pm 0.03$ | 0.04      | 5                                   | 7.40<br>$\pm 0.03$ | 0.02              | Vein                                | 6  | 7.32<br>$\pm 0.05$ | 0.05 |
|                              | F         | 12                                  | 7.34<br>$\pm 0.04$ | 0.06      | 3                                   | 7.29<br>$\pm 0.03$ | 0.01              | Artery                              | 6  | 7.27<br>$\pm 0.08$ | 0.08 |
| Pco <sub>2</sub><br>mm Hg    | M         | 12                                  | 24.7<br>$\pm 2.4$  | 4.0       | 5                                   | 26.9<br>$\pm 6.1$  | 4.8               | V                                   | 6  | 33.1<br>$\pm 3.6$  | 3.5  |
|                              | F         | 12                                  | 42.8<br>$\pm 4.8$  | 7.5       | 3                                   | 41.5<br>$\pm 6.5$  | 2.6               | A                                   | 6  | 42.3<br>$\pm 12.3$ | 11.6 |
| BD <sub>ECF</sub><br>mmol/l  | M         | 12                                  | 5.2<br>$\pm 2.0$   | 3.2       | 5                                   | 7.2<br>$\pm 2.8$   | 2.3               | V                                   | 6  | 8.1<br>$\pm 2.4$   | 2.3  |
|                              | F         | 12                                  | 2.3<br>$\pm 2.6$   | 4.3       | 3                                   | 5.7<br>$\pm 2.5$   | 1.0               | A                                   | 6  | 7.3<br>$\pm 2.2$   | 2.1  |
| SaO <sub>2</sub><br>per cent | F         | 8                                   | 58<br>$\pm 11$     | 13        |                                     |                    |                   | V                                   | 2  | 85<br>$\pm 0$      | 0    |
|                              |           |                                     |                    |           |                                     |                    |                   | A                                   | 3  | 47<br>$\pm 19$     | 8    |

|                       |        |                 |       |  |        |                 |       |
|-----------------------|--------|-----------------|-------|--|--------|-----------------|-------|
| Glucose<br>mg%        | M<br>7 | 91<br>±17       | 18    |  | V<br>4 | 92<br>±46       | 29    |
|                       | F<br>7 | 72<br>±8        | 9     |  | A<br>3 | 81<br>±50       | 20    |
| Lactate<br>mmol/l     | M<br>7 | 2.6<br>±0.9     | 0.9   |  | V<br>4 | 5.3<br>±4.5     | 2.8   |
|                       | F<br>8 | 3.5<br>±2.1     | 2.6   |  | A<br>3 | 4.8<br>±8.2     | 3.3   |
| Pyruvate<br>mmol/l    | M<br>7 | 0.12<br>±0.04   | 0.04  |  | V<br>3 | 0.13<br>±0.16   | 0.07  |
|                       | F<br>7 | 0.11<br>±0.03   | 0.03  |  | A<br>3 | 0.13<br>±0.13   | 0.05  |
| $\beta$ -HB<br>mmol/l | M<br>7 | 1.36<br>±1.17   | 1.26  |  | V<br>4 | 0.60<br>±0.50   | 0.33  |
|                       | F<br>7 | 0.43<br>±0.30   | 0.32  |  | A<br>3 | 0.50<br>±0.65   | 0.25  |
| Glycerol<br>mmol/l    | M<br>7 | 0.154<br>±0.056 | 0.060 |  | V<br>4 | 0.104<br>±0.067 | 0.043 |
|                       | F<br>7 | 0.062<br>±0.018 | 0.018 |  | A<br>3 | 0.068<br>±0.009 | 0.003 |

Table VII. Different maternal (M) and fetal (F) blood components, determined in the first and second stage of labour and in umbilical cord blood in series E (low Apgar score).

Mean values, standard deviations and 95% confidence limits of the means.

|                              | 1st stage |                                     |                    | Late 2nd stage |                                     |                    | Umbilical vessels |                                     |    |                    |      |
|------------------------------|-----------|-------------------------------------|--------------------|----------------|-------------------------------------|--------------------|-------------------|-------------------------------------|----|--------------------|------|
|                              | n         | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 | n              | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd                 | n                 | $\bar{x}$<br>$\pm 95\%$<br>conf lim | sd |                    |      |
| pH                           | M         | 13                                  | 7.48<br>$\pm 0.04$ | 0.06           | 13                                  | 7.44<br>$\pm 0.05$ | 0.08              | Vein                                | 12 | 7.30<br>$\pm 0.06$ | 0.09 |
|                              | F         | 13                                  | 7.32<br>$\pm 0.03$ | 0.06           | 8                                   | 7.24<br>$\pm 0.08$ | 0.11              | Artery                              | 13 | 7.17<br>$\pm 0.08$ | 0.13 |
| Pco <sub>2</sub><br>mm Hg    | M         | 13                                  | 24.2<br>$\pm 2.8$  | 4.6            | 12                                  | 25.6<br>$\pm 2.8$  | 4.4               | V                                   | 12 | 37.9<br>$\pm 5.7$  | 8.9  |
|                              | F         | 13                                  | 41.8<br>$\pm 3.7$  | 6.1            | 8                                   | 49.1<br>$\pm 8.5$  | 10.1              | A                                   | 13 | 53.1<br>$\pm 7.5$  | 12.0 |
| BDECF<br>mmol/l              | M         | 13                                  | 5.3<br>$\pm 1.1$   | 1.9            | 12                                  | 7.1<br>$\pm 1.3$   | 2.0               | V                                   | 12 | 7.2<br>$\pm 2.6$   | 4.0  |
|                              | F         | 13                                  | 3.5<br>$\pm 2.6$   | 4.4            | 8                                   | 6.0<br>$\pm 3.5$   | 4.3               | A                                   | 13 | 8.2<br>$\pm 3.5$   | 5.6  |
| SaO <sub>2</sub><br>per cent | F         | 7                                   | 50<br>$\pm 14$     | 15             | 4                                   | 30<br>$\pm 25$     | 16                | V                                   | 6  | 58<br>$\pm 23$     | 22   |
|                              |           |                                     |                    |                |                                     |                    |                   | A                                   | 7  | 34<br>$\pm 13$     | 14   |

|                    |   |    |                 |       |    |                 |       |   |    |                 |       |
|--------------------|---|----|-----------------|-------|----|-----------------|-------|---|----|-----------------|-------|
| Glucose<br>mg%     | M | 12 | 108<br>±15      | 24    | 11 | 119<br>±12      | 18    | V | 13 | 80<br>±12       | 19    |
|                    | F | 10 | 79<br>±10       | 13    | 7  | 82<br>±24       | 26    | A | 13 | 67<br>±12       | 19    |
| Lactate<br>mmol/l  | M | 12 | 2.4<br>±0.7     | 1.1   | 11 | 6.1<br>±1.3     | 2.1   | V | 13 | 6.6<br>±2.0     | 3.3   |
|                    | F | 11 | 3.3<br>±1.3     | 1.9   | 6  | 8.8<br>±5.4     | 5.0   | A | 12 | 8.2<br>±2.4     | 3.8   |
| Pyruvate<br>mmol/l | M | 12 | 0.13<br>±0.04   | 0.07  | 11 | 0.23<br>±0.07   | 0.11  | V | 12 | 0.18<br>±0.09   | 0.14  |
|                    | F | 10 | 0.10<br>±0.05   | 0.07  | 6  | 0.15<br>±0.09   | 0.09  | A | 13 | 0.18<br>±0.06   | 0.10  |
| β-HB<br>mmol/l     | M | 10 | 1.53<br>±0.68   | 0.96  | 10 | 1.44<br>±0.52   | 0.73  | V | 11 | 1.23<br>±1.02   | 1.52  |
|                    | F | 10 | 0.40<br>±0.18   | 0.26  | 6  | 0.50<br>±0.20   | 0.20  | A | 12 | 0.87<br>±0.70   | 1.12  |
| Glycerol<br>mmol/l | M | 11 | 0.167<br>±0.051 | 0.076 | 11 | 0.199<br>±0.054 | 0.080 | V | 12 | 0.087<br>±0.031 | 0.049 |
|                    | F | 10 | 0.072<br>±0.034 | 0.049 | 7  | 0.093<br>±0.047 | 0.050 | A | 13 | 0.069<br>±0.022 | 0.034 |
| Sodium<br>mmol/l   | M | 6  | 137.3<br>±2.8   | 2.8   | 6  | 137.1<br>±5.7   | 5.4   | V | 7  | 150.7<br>±6.4   | 6.8   |
|                    | F | 8  | 138.7<br>±11.1  | 10.4  | 4  | 143.3<br>±15.6  | 9.8   | A | 8  | 150.4<br>±8.3   | 9.9   |

Table VIII. Different maternal (M) and fetal (F) blood components, determined in the first and second stage of labour and in umbilical cord blood in series F (control series).  
Mean values, standard deviations, and 95 % confidence limits of the means.

|                           | 1st stage |           |            |      | 2nd stage |           |            |      | Umbilical vessels |           |            |      |
|---------------------------|-----------|-----------|------------|------|-----------|-----------|------------|------|-------------------|-----------|------------|------|
|                           | n         | $\bar{x}$ | $\pm 95\%$ | sd   | n         | $\bar{x}$ | $\pm 95\%$ | sd   | n                 | $\bar{x}$ | $\pm 95\%$ | sd   |
| pH                        | M 17      | 7.45      | $\pm 0.02$ | 0.04 | 19        | 7.43      | $\pm 0.02$ | 0.04 | Vein 17           | 7.32      | $\pm 0.02$ | 0.04 |
|                           | F 17      | 7.36      | $\pm 0.02$ | 0.05 | 18        | 7.32      | $\pm 0.03$ | 0.05 | Artery 17         | 7.27      | $\pm 0.03$ | 0.05 |
| Pco <sub>2</sub><br>mm Hg | M 17      | 26.5      | $\pm 2.3$  | 4.4  | 19        | 22.7      | $\pm 1.9$  | 3.9  | V 17              | 35.7      | $\pm 3.6$  | 7.1  |
|                           | F 17      | 38.9      | $\pm 2.8$  | 5.3  | 18        | 39.6      | $\pm 3.8$  | 7.8  | A 17              | 45.5      | $\pm 4.2$  | 8.2  |
| BDECF<br>mmol/l           | M 17      | 4.9       | $\pm 1.3$  | 2.5  | 19        | 8.6       | $\pm 1.1$  | 2.1  | V 17              | 6.9       | $\pm 1.5$  | 3.0  |
|                           | F 17      | 3.7       | $\pm 1.5$  | 2.8  | 18        | 5.0       | $\pm 1.5$  | 2.8  | A 17              | 5.6       | $\pm 1.7$  | 3.3  |



|                       |    |                 |                 |       |                 |                 |   |    |                 |       |
|-----------------------|----|-----------------|-----------------|-------|-----------------|-----------------|---|----|-----------------|-------|
| M                     | 17 | 88<br>±4        | 8               | 17    | 110<br>±11      | 22              | V | 16 | 88<br>±6        | 12    |
| Glucose<br>mg%        | F  | 16              | 71<br>±6        | 11    | 16              | 82<br>±10       | A | 15 | 76<br>±8        | 15    |
| M                     | 17 | 2.8<br>±1.5     | 3.0             | 16    | 5.4<br>±1.5     | 2.7             | V | 17 | 5.2<br>±1.1     | 2.0   |
| Lactate<br>mmol/l     | F  | 17              | 3.2<br>±0.6     | 1.3   | 17              | 4.3<br>±1.1     | A | 17 | 5.4<br>±1.1     | 2.1   |
| M                     | 9  | 0.16<br>±0.09   | 0.12            | 9     | 0.26<br>±0.09   | 0.12            | V | 8  | 0.19<br>±0.09   | 0.11  |
| Pyruvate<br>mmol/l    | F  | 10              | 0.13<br>±0.05   | 0.06  | 8               | 0.19<br>±0.07   | A | 8  | 0.21<br>±0.09   | 0.10  |
| M                     | 14 | 0.99<br>±0.73   | 1.26            | 14    | 1.97<br>±0.71   | 1.23            | V | 12 | 0.76<br>±0.29   | 0.46  |
| $\beta$ -HB<br>mmol/l | F  | 14              | 0.34<br>±0.24   | 0.41  | 13              | 0.63<br>±0.20   | A | 11 | 0.60<br>±0.22   | 0.32  |
| M                     | 17 | 0.159<br>±0.025 | 0.049           | 15    | 0.238<br>±0.028 | 0.051           | V | 16 | 0.094<br>±0.014 | 0.026 |
| Glycerol<br>mmol/l    | F  | 17              | 0.069<br>±0.013 | 0.026 | 16              | 0.086<br>±0.017 | A | 14 | 0.075<br>±0.013 | 0.023 |

The mean value of the lactate/pyruvate ratio (L/P ratio) in the fetal blood was calculated to be, in the first stage of labour, 27 in Group A, 28 in Group B, 34 in Group C, 33 in Group D, and 32 in Group E. In the second stage, the fetal mean L/P ratio was 32, 39, and 41 in the Groups A, B, and C, and 50 in Group E. In the control group, the corresponding mean values were 28 and 27, respectively. None of the differences between the groups were statistically significant.

Plasma  $\beta$ -hydroxybutyrate (Tables III-VIII). In the first and also in the second stage of labour, the mean maternal  $\beta$ -hydroxybutyrate values exceeded the mean fetal values by 0.5-1.3 mmol/l. The maternal mean values were within the range of 0.7-1.5 mmol/l, and the fetal means within the range of 0.2-0.6 mmol/l. The mean concentration of  $\beta$ -hydroxybutyrate was generally higher in the second stage of labour than in the first. No significant differences were present between the corresponding mean values of the different groups. In all the groups, the umbilical venous blood showed a somewhat higher mean level of  $\beta$ -hydroxybutyrate than the umbilical arterial blood.

Plasma glycerol (Tables III-VIII). In all groups, the maternal plasma glycerol mean concentration was higher in the second stage of labour than in the first (the range of means being 0.199-0.242 mmol/l and 0.122-0.170 mmol/l, respectively). The greatest difference between the stages of labour was seen in the control group. The only statistically significant difference between the groups was found between Group B (fetal bradycardia and passage of meconium) and the controls in the second stage of labour ( $p < 0.01$ ), the value in the former being lower.

The fetal mean values were throughout lower than the corresponding maternal ones, the maternal-fetal difference being around 0.10-0.15 mmol/l. Similar to the maternal glycerol mean levels, the fetal mean values were somewhat higher in the second stage of labour than in the first, the highest value being seen in the control group. No significant differences were encountered between the groups concerning the fetal means of glycerol.

The mean values in umbilical venous blood were in all groups 0.01-0.03 mmol/l higher than the corresponding values in arterial blood, the difference being statistically significant in all groups. A comparison of all groups showed that the lowest means of umbilical cord blood glycerol (0.064 mmol/l in venous, and 0.055 mmol/l in arterial blood) were in Group B. These mean values differed significantly from the corresponding means in the control group ( $p < 0.01$  for the venous, and  $p < 0.05$  for the arterial blood results).

Plasma sodium (Tables III, IV, V, and VII). Plasma sodium was determined in Groups A (passage of meconium), B (fetal bradycardia and passage of meconium), C (fetal bradycardia), and E (low Apgar score). In all these groups, the mean values of maternal and also of fetal plasma sodium concentration were around 140 mmol/l in both the first and second stage of labour. In umbilical venous blood, the mean value in Group E was somewhat higher than in the remaining groups, the difference between Group E (150 mmol/l), on the one hand, and Groups A and B (143 mmol/l), on the other, being statistically significant ( $p < 0.05$ ).

## COMMENTS

The 72 cases included in the present investigation were very carefully selected to ensure a high homogeneity in each subgroup concerning the specific clinical sign of fetal distress defining the group in question. However, a certain degree of bias is unavoidable in clinical studies of delivery cases and must be taken into account in evaluating the biochemical significance of the different diagnostic signs and also in comparing the results with those of other investigations.

A prominent feature of this material was that, despite the clinical signs being very pronounced in many of the cases, the majority of the infants were vigorously born, and that, in those that were depressed at birth, the depression was moderate and easily treated by simple resuscitation procedures. In no instance was serious asphyxia encountered. As such cases are extremely rare at this department, the present material is representative of the diagnostic situations and problems generally met with in suspected fetal distress.

A comparison of the different clinical signs with regard to their biochemical significance, revealed that passage of meconium only, i.e. without any FHR disturbances (Group A), showed the least deviation from the normal control group concerning all acid-base and metabolic components studied. Two infants of this group were depressed at birth. In one of them a very low pH (7.06) and high  $\Delta\text{pH}$  and  $\text{BD}_{\text{ECF}}$  values were recorded in the second stage of labour, whereas in the other, a  $\Delta\text{pH}$  of 0.17 in the second stage was the only noticeable biochemical finding. The absence of FHR irregularities in the former case is remarkable and might be considered doubtful for the terminal phase of labour. However, it would seem that meconium-staining of the amniotic fluid, no FHR disturbances being present, was generally related to no or slight fetal and maternal meta-

bolic changes and to a favourable fetal prognosis. This agrees with the opinion expressed by i.a. Berg et al. (1970) and Tipton & Shelley (1971).

The association of meconium-stained amniotic fluid and periods of fetal bradycardia (Group B) in this study showed the highest frequency of depressed infants at birth (5/20) to judge from the Apgar score. Biochemically, this group was characterized by rather moderate changes. In fetal scalp blood, no pH values  $< 7.20$  were found, but in the second stage of labour, a somewhat raised frequency of  $\Delta\text{pH}$  values  $\leq 0.15$  units was noted. The fetal  $\text{Pco}_2$  mean value found in the second stage, although only moderately increased (48 mm Hg), was significantly higher than in the control group. The fetal L/P ratio was somewhat increased in the first and also in the second stage compared with the normal series. If the results of this group were analysed together with those of Group C, denoting fetal bradycardia only, the frequency of  $\Delta\text{pH}$  values  $\geq 0.15$  pH units was found to be significantly higher than in the control group, the same applying to the frequency of pH values  $< 7.20$  in umbilical arterial blood at birth. It is noteworthy that the fetal plasma glycerol concentration in the second stage was on average lower than in the remaining groups, which contrasts to a report given by Šabata et al. (1970) who found increased plasma glycerol concentrations in umbilical cord blood where there was fetal distress. However, the significance of fetal plasma glycerol is still very uncertain, and in a previous study on fetal bradycardia after paracervical block anaesthesia, our results on this point were more in accordance with those of Šabata (Gårdmark et al. 1974 b).

In the group presenting fetal bradycardia only (Group C), more pronounced biochemical changes were recorded than in the preceding group, presenting the combination of fetal bradycardia and passage of meconium. It might be questioned whether this is a real or a seeming difference, i.e. appearing by chance owing to variations inherent in the significance of fetal bradycardia as a sign of fetal distress. It should be noted that only two infants out of 16 in Group C were depressed at birth, as opposed to five out of 20 in Group B.

The biochemical changes in the fetal bradycardia group included an increased frequency of pH values  $\leq 7.20$  in the second stage of labour, and of  $\Delta\text{pH}$  values  $\geq 0.20$  units in the first and second stage, compared with the normal group. Six of the 14 infants in whom pH of the umbilical artery blood was determined had a value  $< 7.15$ . In the second stage of labour, the fetal  $\text{Pco}_2$  mean level (54 mm Hg) was higher than in any of the other groups. The fetal  $\text{BD}_{\text{ECF}}$  values were rather scattered, no single value exceeding 10 mmol/l. However, the frequency of fetal  $\text{BD}_{\text{ECF}}$  exceeding the corresponding maternal  $\text{BD}_{\text{ECF}}$  value (negative  $\Delta\text{BD}_{\text{ECF}}$ ) tended to



be somewhat higher in this group than in the remaining groups. Furthermore, this group included comparatively higher mean levels of fetal plasma lactate, and in the first stage, a somewhat lower mean value of the fetal blood oxygen saturation. The fetal blood determinations thus clearly indicated a relatively high frequency of acidotic fetuses in this group.

The maternal blood composition in Group C showed a feature somewhat deviating from that of the remaining groups in the sense of higher pH mean levels and lower mean values of  $P_{CO_2}$ , most obvious in the first stage of labour. These findings indicate a pronounced hyperventilation and are interesting in view of the correlation between excessive maternal hyperventilation and impaired fetal gas exchange suggested by several authors (Moya et al. 1965; Morishima et al. 1965; Trüber & Saling 1972).

The prognostic and biochemical significance of fetal tachycardia has been differently interpreted. It has been considered a sign strongly indicating fetal distress (Caldeyro-Barcia et al. 1966; Coltart et al. 1969), sometimes indicating fetal distress (Kubli et al. 1969; Wood et al. 1969; Beard et al. 1971; O'Gureck et al. 1972), or not indicating impaired fetal oxygenation (Hobel 1971). Those authors who considered fetal tachycardia a relative indicator of fetal asphyxia have suggested two types of tachycardia: baseline tachycardia, being an innocuous sign, and tachycardia associated with periods of deceleration, being a more serious sign.

In the present study, the fetal tachycardia cases (Group D) showed no or only slight deviation from the normal controls concerning the fetal and maternal blood composition. The present cases being characterized by a baseline tachycardia, often persistent for a long period but not associated with FHR decelerations, the results obtained seem to confirm the mentioned opinion that fetal tachycardia alone is not generally related to fetal metabolic disturbances.

In order to evaluate the biochemical significance of low one-minute Apgar score, a group of 14 cases scoring 7 or less, and mainly selected from the other groups of the investigation, was subjected to analysis. The biochemical changes seen in this group were mainly related to the acid-base components of the fetal blood, in particular to pH and  $\Delta pH$ . The mean values of pH in both the first and second stage of labour were lower than those of the remaining groups, being 7.24 in the second stage. But the range of the single values was rather wide. The frequency of pH values  $\leq 7.20$  was significantly higher than in the control series, as was the frequency of  $\Delta pH \geq 0.20$  units. The pH mean of umbilical artery blood (7.17) was the lowest found throughout the groups. The mean levels of  $BD_{ECF}$  was somewhat higher in the second stage and in umbilical arterial blood at birth than in the controls, although not to a significant degree.



The average fetal plasma lactate concentration was low in the first stage, but was considerably increased in the second, as was the L/P ratio. Although the mean oxygen saturation of the fetal blood in the second stage of labour was lower than in the remaining groups, the difference was not statistically significant.

The overall results obtained in the low Apgar score group clearly indicate that several of these infants were in a state of metabolic acidosis due to impaired oxygen supply, the degree of acidosis being on average moderate, which correlated well with the moderate depression actually presented. It should be noted that, according to the design of this investigation, the results related to the first and second stage of labour, respectively, are not really expressing intra-labour changes in the single cases, as the cases analysed in the first and second stage within each group are not identical. The results therefore indicate the biochemical conditions specifically existing at the appearance of the different clinical signs in the first or the second stage. The differences of results found between the two stages should, to a certain extent, be considered "normal" changes generally occurring during labour; they might also be because the time interval between sampling and delivery was on average shorter in those cases investigated in the second stage. In other words, it could be that the predictive value of fetal and maternal blood determinations is inversely correlated with the sampling-delivery interval.

In addition to these considerations, the results obtained in some of the single cases of the low Apgar score group underline the known fact that the Apgar score can be lowered by factors other than impairment of the oxygen supply and related metabolism. As pointed out by Beard *et al.* (1971), it is reasonable to suppose that vital damage to the fetus, particularly to the CNS, is unlikely to occur before there is metabolic evidence of oxygen depletion. It would be desirable therefore to include biochemical evaluation into the routine assessment of the newborn child condition currently based on Apgar scoring alone. (This is further discussed below.)

In accordance with the aim of the present investigation, the results obtained should also be considered from another point of view; namely, with regard to the proportionate informative value of the different biochemical variables. It is not possible from this study to discuss whether clinical signs precede biochemical changes, or vice versa. But the results indicate that in groups of cases, defined by the presence of different clinical signs of suspected fetal distress and thus including a certain, though not exactly known, number of true fetal distress conditions, the biochemical changes found are mainly related to the acid-base balance and the plasma lactate concentration. A consideration of these changes in detail suggests

that in the main, they are definable by two variables, fetal pH and the maternal-fetal pH difference ( $\Delta\text{pH}$ ). The discriminative value of  $\text{BD}_{\text{ECF}}$  was low because of the wide-ranged distribution of single values within each group. The same applied to the maternal-fetal  $\text{BD}_{\text{ECF}}$  difference ( $\Delta\text{BD}_{\text{ECF}}$ ) disagreeing with results obtained in some other investigations (Beard *et al.* 1968; Vretos 1970; Roversi & Canussio 1970; Seidenschnur & Heinrich 1973). However, in the group showing the most pronounced biochemical changes, i.e. the fetal bradycardia group, some negative  $\Delta\text{BD}_{\text{ECF}}$  values were seen (cf. Seidenschnur & Heinrich 1973). Fetal  $\text{Pco}_2$  values were not found to present any significant pattern of distribution within the different groups. Only in the fetal bradycardia group were a few single values above 60 mm Hg encountered in the second stage of labour, this figure being considered the upper normal limit by Lumley *et al.* (1971). Of the remaining metabolic components determined in this study, plasma lactate determinations undoubtedly yield additional information in cases of fetal metabolic acidosis. Owing to the more complicated and time-consuming assay technique, lactate determination would seem out of the question in clinical practice.

To sum up: the results of the present study strongly favour the view, previously advanced (cf. Jacobson 1970; Jacobson & Rooth 1971; Rooth *et al.* 1973; Seidenschnur *et al.* 1973; Seidenschnur & Heinrich 1973; Jacobson *et al.* 1974), that routine biochemical assessment of the intrauterine condition of the fetus during labour should not rely on fetal pH alone, but should include the simultaneous determination of maternal pH, and thus of the  $\Delta\text{pH}$ . Such pH determinations, being technically simple, in association with FHR monitoring would currently seem to offer the best alternative for supervision of the fetus in labour possible to adopt at most obstetrical wards. The additional information obtainable from determinations of other acid-base and metabolic components, although of high interest in research studies, would seem too limited for average clinical purposes to justify the considerable increase in work, equipment, and personnel then required. However, it might additionally be suggested that determination of pH in umbilical artery blood of the clamped cord at birth are successively made a routine, at least in high-risk delivery cases, to extend the possibilities of assessing the state of the newborn infant (cf. Kubli *et al.* 1972).

## SUMMARY

A total series of 72 parturients presenting different clinical signs of fetal distress during labour and 19 normal controls were subjected to analysis of the fetal and maternal blood biochemistry related to the various signs. The determinations included pH,  $\text{Pco}_2$ ,  $\text{BD}_{\text{ECF}}$ ,  $\text{SaO}_2$ , plasma glucose, lactate, pyruvate,  $\beta$ -hydroxybutyrate, glycerol, and sodium.

The 72 were divided into four groups, strictly defined according to the presence of the following clinical signs of suspected fetal distress: A) passage of meconium, B) fetal bradycardia + passage of meconium, C) fetal bradycardia only, D) fetal tachycardia. In addition, those in Groups A-D (+ a few additional) where the infants presented a low one-minute Apgar score were subjected to separate analysis (Group E). There were 11 depressed infants in Groups A-D. The entire material may be considered representative of such moderate fetal distress conditions mainly encountered at this clinic, very severe cases of fetal asphyxia being rare.

The most pronounced biochemical changes, compared with the control series, were seen in the two fetal bradycardia groups (Group B and C), the group comprising cases with fetal bradycardia alone (Group C) showing the most dominant changes. Fetal bradycardia, with or without meconium-staining of the liquor, related to a raised frequency of fetal metabolic acidosis, i.e. changes in the fetal acid-base components and the plasma lactate concentration. No significant changes between the groups were found in plasma glucose,  $\beta$ -hydroxybutyrate, glycerol or sodium. The  $\text{SaO}_2$  of fetal blood was moderately but non-significantly lowered in Group C.

No or slight biochemical deviations from the normal were found in those presenting meconium-stained amniotic fluid (Group A) or in those with fetal tachycardia (Group D).

The low Apgar score cases (Group E) were characterized by a high incidence of metabolic acidosis in fetal scalp blood and umbilical arterial blood. The predictive value of fetal scalp blood analysis was suggested to increase inversely with the sampling-delivery time interval. Several of the depressed infants showed no abnormal biochemical pattern.

The different biochemical variables determined were evaluated with regard to their informative significance. It was concluded that, for routine clinical purposes, reliable information of the fetal metabolic status is obtainable by measuring fetal pH and the maternal-fetal pH difference ( $\Delta\text{pH}$ ), the latter often yielding the most important information. It is implied that biochemical supervision during labour should be routinely associated with FHR monitoring.

To reduce the inaccuracy inherent in the common method of assessing the newborn child condition by means of Apgar scoring only, it is proposed that determination of pH in the umbilical artery blood in the clamped cord at birth be made a routine, at least in high-risk delivery cases.

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THEORETICAL ASPECTS ON THE MATERNAL-FETAL pH-DIFFERENCE  
( $\Delta$  pH), DETERMINED DURING LABOUR

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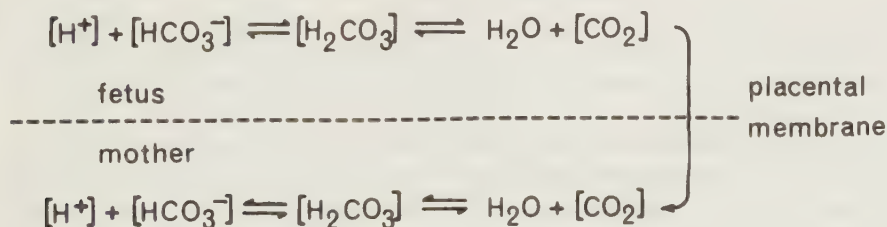


Biochemical monitoring of the fetus during labour by means of scalp blood analyses is increasingly adopted as a routine in clinical obstetrics. However, opinions differ on which blood determinations yield the most reliable and prompt information of the fetal intrauterine condition. It would seem that pH of the fetal blood, sometimes in combination with pH of maternal blood, is the parameter usually chosen.

In previous reports, we and others have advocated that calculation of the maternal-fetal pH difference ( $\Delta$  pH) will add substantially to the informative value of acid-base balance determinations (cf. Jacobson 1970; Jacobson & Rooth 1971; Khazin & Hon 1971 a & b; Heinrich *et al.* 1972; Rooth *et al.* 1972, 1973; Seidenschnur *et al.* 1973; Gårdmark *et al.* 1974 a & b) brief summary of these studies shows that in normal labour conditions the  $\Delta$ pH value will generally remain stable between 0.10 and 0.15 pH units. An increased  $\Delta$  pH value between 0.15–0.20 pH units should be considered a warning sign of a beginning fetal metabolic acidosis indicating imminent fetal hypoxia, and a  $\Delta$  pH value above 0.20 pH units should be regarded as a marked sign of abnormal fetal conditions.

Although, from a practical point of view, these statements are valid within the normal pH-range,  $\Delta$ pH calculations imply a certain inadvertency, as is evident from the following reasoning.

The major product of the fetal metabolism is the  $H^+$  ions, formed when the metabolic generated  $CO_2$  reacts with the cellular water. The main way for the fetus to eliminate its surplus of  $H^+$  ions is by reversal of  $CO_2$  formation and diffusion of  $CO_2$  through the placenta to the maternal blood, where  $H^+$  ions will again be formed by the opposite reaction. The mechanism can be simply expressed:



The formula clearly illustrates the important relation between the fetal and the maternal  $H^+$  ion concentration, and hence the importance of  $\Delta$ pH determinations. However, because the pH denotes the negative logarithm of the  $H^+$  ion concentration,  $\Delta$ pH might under certain circumstances be misleading as an expression of the difference between the maternal and the fetal  $H^+$  ion concentration. This can be found by transforming different pH values within the biological range into  $H^+$  ion concentration values, and



calculating the maternal-fetal difference of  $H^+$  ion concentration ( $\Delta [H^+]$ ) at these different pH values.

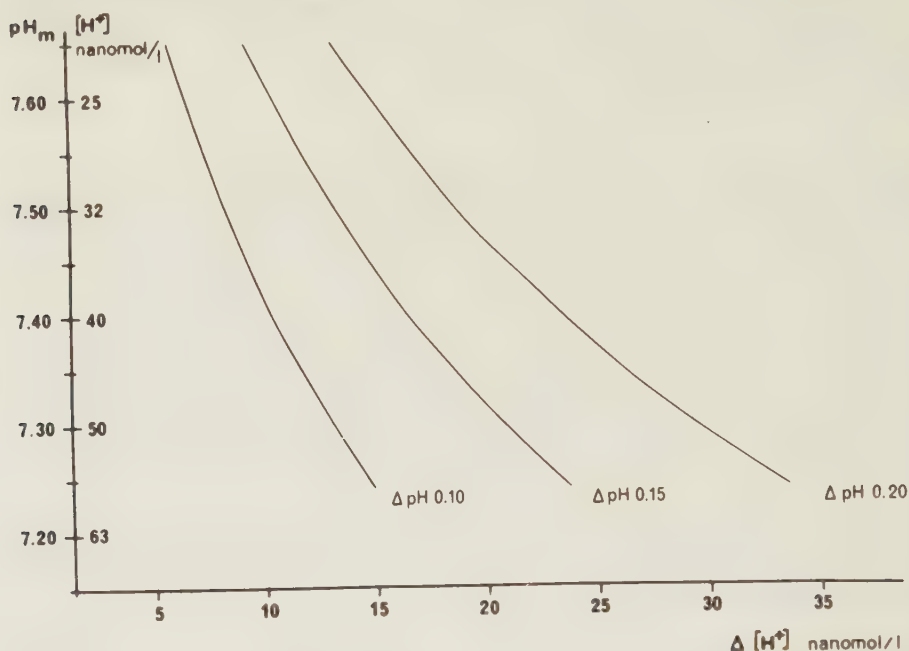


Fig. 1. Nomogram for calculation of the maternal-fetal  $[H^+]$ -concentration difference ( $\Delta [H^+]$ ) at different maternal-fetal pH differences (different  $\Delta pH$  values).  $pH_m$  = actual maternal pH.

The nomogram given in Fig. 1 was constructed on the basis of such calculations. From this nomogram, the  $\Delta [H^+]$  can be derived at three different  $\Delta pH$  values (0.10, 0.15, and 0.20 pH units). As seen, the relation between  $\Delta pH$  and  $\Delta [H^+]$  is such that at high maternal pH levels the  $\Delta pH$  may be increased with no/or small change in the maternal-fetal difference of  $H^+$  ion concentration. At low maternal pH values, the opposite is true. Thus, for instance, the  $\Delta [H^+]$  at a maternal pH of 7.40 and a fetal pH 7.30 ( $\Delta pH = 0.10$ ) is equal (approximately 10 nanomol/l) to the  $\Delta [H^+]$  at a maternal pH of 7.60 and a fetal pH of 7.45 ( $\Delta pH = 0.15$ ).

The practical relevance of these facts may be illustrated by the results obtained in a double-blind study of the effects of paracervical block on the maternal and fetal acid-base balance, previously reported by us (Gårdmark, Jacobson & Rooth 1974). In that series of cases, there was a high frequency of hyperventilating mothers, presenting very low  $P_{CO_2}$  values and thus unusually high values of pH. From the series, 11 cases with a maternal pH  $\geq 7.55$  could be derived.

Table I. Maternal and fetal pH value and corresponding  $\Delta$ pH and  $\Delta$  H<sup>+</sup>ion concentration in a series of hyperventilating mothers during labour (see text).

| Maternal pH    | Fetal pH | $\Delta$ pH | $\Delta$ [H <sup>+</sup> ] |
|----------------|----------|-------------|----------------------------|
| 7.62           | 7.44     | 0.18        | 12.3                       |
| 7.56           | 7.29     | 0.27        | 23.8                       |
| 7.60           | 7.41     | 0.19        | 13.8                       |
| 7.56           | 7.42     | 0.14        | 10.5                       |
| 7.55           | 7.38     | 0.17        | 13.5                       |
| 7.56           | 7.39     | 0.17        | 13.2                       |
| 7.56           | 7.39     | 0.17        | 13.2                       |
| 7.55           | 7.43     | 0.12        | 9.0                        |
| 7.62           | 7.30     | 0.32        | 26.1                       |
| 7.56           | 7.33     | 0.23        | 19.3                       |
| 7.56           | 7.40     | 0.16        | 12.3                       |
| $\bar{x}$ 7.57 | 7.38     | 0.19        | 14.0                       |

Table 1 gives the individual pH values of these mothers together with the corresponding fetal pH values. All the determinations were made before the paracervical block was administered or refer to the control group receiving saline. Clinically, these patients and their fetuses were in all respects normal.

As the Table shows, the mean  $\Delta$ pH value was found to be 0.19 pH units at a mean maternal pH of 7.57. Of the individual  $\Delta$ pH values, all except two exceeded 0.15 pH units. The nomogram in Fig. 1 shows that the  $\Delta$ [H<sup>+</sup>] at the mean values given in Table I are approximately 15 nanomol/l. The  $\Delta$ [H<sup>+</sup>] value would have been the same at a maternal pH of 7.44 and a  $\Delta$ pH value of 0.15 pH units.

As previously mentioned, the  $\Delta$ pH value yields very good information in addition to maternal and fetal pH determinations *per se*, and in most cases met with in practice, it would seem that the considerations mentioned in this paper are of less relevance, as the general range of maternal pH lies

between approximately 7.35 and 7.45. At more extreme maternal pH values, either very high or very low, the true difference of  $H^+$  ion concentration should be taken into account, however, when interpreting the  $\Delta pH$  value.

## SUMMARY

The informative value of the maternal-fetal pH difference ( $\Delta pH$ ) value in the biochemical monitoring of the fetus during labour has previously been reported on and is again emphasized. However, theoretically the  $\Delta pH$  value will vary as an expression for the true maternal-fetal difference of the  $H^+$  ion concentration at different pH levels. This can be seen at very high and very low maternal pH values and should then be taken into account when stating numerical limits of the  $\Delta pH$  value between normal and abnormal fetal conditions. A nomogram of the relation between  $\Delta pH$  and the maternal-fetal difference of  $H^+$  ion concentration ( $\Delta [H^+]$ ) is presented and may be a guide at the interpretation of  $\Delta pH$  in such instances.

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